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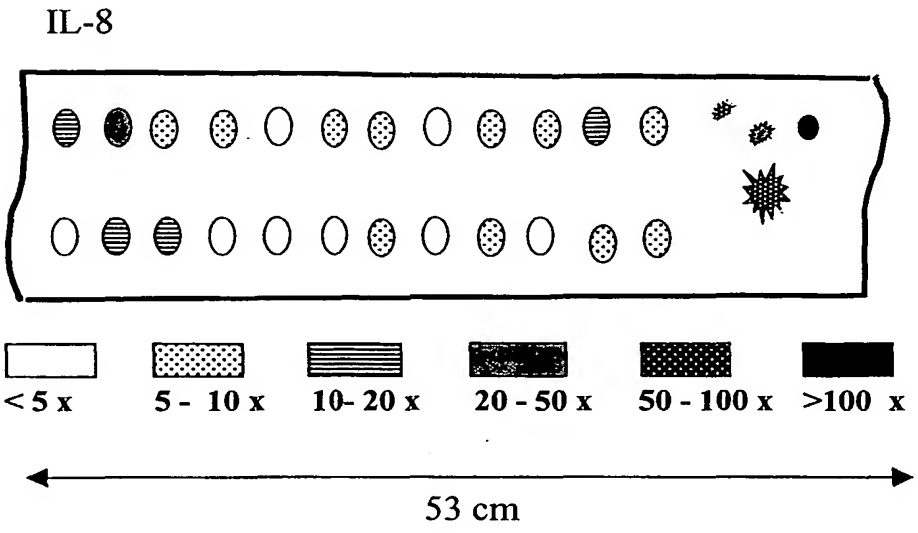
(54) Title: BIOMARKER PANEL FOR COLORECTAL CANCER



(57) Abstract: A panel of biomarkers has been identified for analysis of colorectal cancer. The panel, originally identified using a mouse colon cancer model, has been used to assess changes in human tissue from surgical and biopsy samples against a normal human control panel of biomarkers. The panel may be used for providing a cost effective, rapid, noninvasive procedure for risk assessment, early diagnosis, establishing prognosis, monitoring patient treatment, detecting relapse, and for the discovery of therapeutic intervention of colorectal cancer.

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BIOMARKER PANEL FOR COLORECTAL CANCER

Reference to Related Applications

This application claims priority to U.S. Provisional Patent Application 60/488,660 entitled Molecular Marker Panel for Determination of Colorectal Cancer, by Nancy M. Lee et al., filed July 18, 2003 (Attorney Docket CPMC-01000US0); and U.S. Patent Application 10/690,880 entitled Biomarker Panel for Colorectal Cancer, by Nancy M. Lee et al., filed October 22, 2003 (Attorney Docket CPMC-01000US1), both of which are incorporated herein by reference.

Background

The field of art of this disclosure concerns biomarkers for colorectal cancer (CRC). These biomarkers are useful for risk assessment, early detection, establishing prognosis, evaluation of intervention, recurrence of CRC, and discovery of therapeutic intervention, and methods of use thereof.

In the field of medicine, clinical procedures providing for the risk assessment and early detection of CRC have been long sought. Currently, CRC is the second leading cause of cancer-related deaths in the Western world. One picture that has clearly emerged through decades of research into CRC is that early detection is critical to enhanced survival rates.

The currently accepted methods for CRC screening include the fecal occult blood test (FOBT), x-ray using double contrast between barium enema and air (DCBE), sigmoidoscopy, and colonoscopy. Sigmoidoscopy is an invasive procedure that visually examines the lower third of the colon using a lighted, flexible endoscope, while a related method, colonoscopy, is a procedure that examines the entire colon. In both cases, biopsy samples can be taken during the procedure.

Concerning the accepted methods for screening, none clearly possess what is desired in a screening examination for CRC. While FOBT is

rapid, it is a very general, and therefore a very non-specific screening method for CRC. Though DCBE has proven useful in specifically imaging abnormalities in the colon, the drawbacks of the DCBE method include: 1.) Patient discomfort in preparation of and during the examination, creating reluctance for compliance of DCBE as a screening method. 2.) Exposure of a patient to x-ray radiation, limiting DCBE in terms of frequency of use as a screening method. 3.) Research indicating that DCBE is more effective in detecting larger growths, which contraindicates its use for early detection. 4.) Biopsy samples cannot be taken during the procedure. 5.) Due to the cost involved, not all insurance providers pay for DCBE screening exams. Though sigmoidoscopy has gained favor from many physicians, the drawbacks of this method include: 1.) Patient discomfort in preparation of and during the examination, creating reluctance for compliance of sigmoidoscopy as a screening method. 2.) Due to the cost involved, not all insurance providers pay for sigmoidoscopy screening exams. 3.) Since only the lower third of the colon is inspected, there is a suggestion by studies that many significant lesions are in the proximal end of the colon, rendering sigmoidoscopy inadequate. Though colonoscopy addresses the issue of complete inspection of the colon, the drawbacks of colonoscopy as a screening method include: 1.) Creating even more patient discomfort than sigmoidoscopy, therefore generally requiring sedation, and thereby exacerbating the issue with patient compliance. 2.) Due to the cost involved, not all insurance providers pay for colonoscopy screening exams. 3.) There are risks of colonoscopy that include bleeding, and puncture of the lining of the colon.

Emerging spectroscopic technologies, such as magnetic resonance imaging and tomographic imaging each have drawbacks that are drawn from the list of drawbacks for the currently accepted screening methodologies.

Accordingly, there is a need in the art for approaches that have value in early detection and treatment of CRC that are cost effective, rapid, and

minimally or noninvasive. Additional utility would be realized from an approach that would also serve as the basis for establishing prognosis, monitoring patient treatment, and detecting relapse, as well as the discovery of therapeutic intervention of CRC.

Brief Description of Figures

FIG 1 is a summary of the sequence listings.

FIGS 2A-2C show data that illustrate a panel of biomarkers for samples taken from adenomous polyps, and suspect tissues vs. normal controls. FIGS 2A-2B are tables that compare the results of model studies done in mouse (2A) for a selection of members of the set of 22 biomarkers listed in the sequence listings with the comparable selection in of biomarkers for human subjects (2B).FIG 2C shows the multivariate analysis for 9 markers for 78 biopsies taken from 12 normal patients and 63 biopsies taken from 6 patients with CRC.

FIGS 3B-3C show expression levels for representative biomarkers, IL-8 (3A), CXCR-2 (3B), and COX-2 (3C) for a series of samples taken from a human subject comparing a histologically identified cancerous lesion, a polyp, and an adjacent non-cancerous tissue vs. a normal control.

FIGS 4A-4C show the results of multiple analysis across a 53 cm distance of a colon for a patient with CRC: 4A shows expression levels for IL-8; 4B shows expression levels for C0X-2; and 4C shows expression levels for CXCR-2.

Detailed Description

Still another sought after approach apart from currently accepted methods for screening for CRC, has been the search for biomarkers that have value in detection and treatment of CRC. For more than four decades, since the discovery of alpha-fetoprotein (AFP) and carcinogenic embryonic antigen (CEA), the search for biomarkers for cancer detection and treatment in general has been in a state of evolution. Biomarkers for cancer have five potential uses in the management of patient care. Ideally, they would be

used for risk assessment, for early diagnosis, for establishing prognosis, for monitoring treatment, and for detecting relapse. Additionally, such markers could play a valuable role in developing therapeutic interventions.

It is further advantageous for the sampling methods used in conjunction with biomarker analysis to be minimally invasive or non-invasive. Examples of such sampling methods include serum, stool, swabs, and the like. Non-invasive and minimally invasive methods increase patient compliance, and generally reduce cost.

Clinically, the two criteria that are important for assessing the effectiveness of biomarkers are selectivity and sensitivity. Selectivity of a biomarker defined clinically refers to percentage of patients correctly diagnosed. Sensitivity of a biomarker in a clinical context is defined as the probability that the disease is detected at a curable stage. Ideally, biomarkers would have 100% clinical selectivity and 100% clinical sensitivity. To date, no single biomarker has been identified that has an acceptably high degree of selectivity and sensitivity required to be effective in for the broad range of needs in patient care management. However, from the clinical perspective, single serum biomarkers, such as AFP and CEA have proven to provide value in some aspects of patient care management.

For example, elevated serum levels of CEA were first discovered in 1965 in patients with adenocarcinoma of the colon. Elevated levels can be found in a variety of benign and malignant conditions other than colon cancer. Additionally, the production of CEA by early localized tumors of the colon is in the normal range. Therefore CEA lacks both the sensitivity and selectivity required to be of value for risk assessment or early diagnosis. Further, elevated levels of CEA correlate poorly with colon tumor differentiation and stage, rendering CEA as a biomarker for prognosis of colon cancer of limited value. The two areas for which CEA has proven helpful clinically in managing patient care are in evaluating the effectiveness of treatment, and for detecting relapse. Illustrative of this, numerous studies

have found that there is high correlation between elevated serum levels of CEA preceding clinical detection of recurrence of colon cancer. This has proven to be of value in managing the care of high-risk patents with second-look surgical procedures based on rising levels of CEA.

Currently, investigations across numerous areas of oncology research, including CRC, ovarian, breast, and head and neck, are finding increased sensitivity and selectivity in panels of markers. It is now generally held that many mutations must take place before normal cell processes are altered, resulting in a disease, such as cancer. Still, given the complexity of biological systems, discovery of panels useful in providing value in patient care management for CRC is in the nascent stage.

To date, a greater understanding of the biology of CRC has been gained through the research on adenomous polyposis coli (APC), p53, and Ki-ras genes, as well as the corresponding proteins, and related pathways involved in the regulation thereof. However, there is a distinct difference between research on a specific a gene, its expression, protein product, and regulation, and understanding what genes are critical to include in a panel used to for the analysis of CRC that is useful in the management of patient care for the disease. To date, panels that have been suggested for CRC are comprised of specific point mutations of APC, p53, and Ki-ras, as well as BAT-26, which is a gene that is a microstatelite instability marker.

What is disclosed herein is based on studies conducted in mouse multiple intestinal neoplasia (MIN) model, in which expressions levels of genes were screened in adenomous polyps. In the mouse MIN subjects, a chemically induced mutation of the APC gene is effected. The normal control is defined by littermates for which there was no aberration of the APC gene, and are therefore designated wildtype. From studies based on the mouse MIN model, candidate genes were selected for studying human subjects. From these human subject studies, a panel of biomarkers is disclosed herein. Further, what is disclosed are methods for measuring gene and

protein expression levels based on the panel. Additionally, another aspect of what is disclosed are kits which provide the reagents and instructions for measuring gene and protein expression levels based on the panel. The panel, methods and kits are useful in the management of patient care for CRC. Additionally, the panel, methods, and kits are believed useful as the basis for discovery of therapeutic interventions for CRC.

FIG 1 is a table that gives an overview of the sequence listing for the disclosed biomarkers. The combination of biomarkers disclosed forms the basis for monitoring CRC with enhanced selectivity and sensitivity, and therefore providing enhanced management of patient care for CRC. It is to be understood that fragments and variants of the biomarkers described in the sequence listings are also useful biomarkers in a panel used for the analysis of CRC. What is meant by fragment is any incomplete or isolated portion of a polynucleotide or polypeptide in the sequence listing. It is recognized that almost daily, new discoveries are announced for gene variants, particularly for those genes under intense study, such as genes implicated in diseases like cancer. Therefore, the sequence listings given are exemplary of what is now reported for a gene, but it recognized that for the purpose of an analytical methodology, variants of the gene, and their fragments are also included.

One embodiment of what is disclosed is a panel of biomarkers with the selectivity and sensitivity required for managing patient care for CRC. In Table 1, entries 1-22 are the polynucleotide coding sequences for a panel of biomarkers, and include the name and abbreviation of the gene. Entries 23-44 in Table 1 are the protein, or polypeptide, amino acid sequences that correspond to the coding sequences for entries 1-22. A biomarker, as defined by the National Institutes of Health (NIH) is a molecular indicator of a specific biological property; a biochemical feature or facet that can be used to measure the progress of disease or the effects of treatment. A panel of biomarkers is a selection of biomarkers. Biomarkers may be from a variety of

classes of molecules. As previously mentioned, there is still a need for biomarkers for CRC having the selectivity and sensitivity required to be effective for all aspects of patient care management. Therefore, the selection of an effective set of biomarkers is differentiating in providing the basis for effective determination of CRC.

In another embodiment of this disclosure, expression levels of polynucleotides for the biomarkers indicated in SEQ ID NOs 1-22, are used in the determination of CRC. Such analysis of polynucleotide expression levels is frequently referred to in the art as gene expression profiling. In gene expression profiling, levels of mRNA in a sample are measured as a leading indicator of a biological state, in this case, as an indicator of CRC. One of the most common methods for analyzing gene expression profiling is to create multiple copies from mRNA in a biological sample using a process known as reverse transcription. In the process of reverse transcription, the mRNA from the sample is used to create copies of the corresponding DNA sequence from which the mRNA was originally transcribed. In the reverse transcription amplification process, copies of DNA are created without the regulatory regions in the gene known as introns. These multiple copies made from mRNA are therefore referred to as copy DNA, or cDNA. Entries 45-88 are the sets of primers used in the reverse transcription process for each gene listed in entries 1-22.

Since the reverse transcription procedure amplifies copies of cDNA proportional to the original level of mRNA in a sample, it has become a standard method that allows the analysis of even low levels of mRNA present in a biological sample. Genes may either be up regulated or down regulated in any particular biological state, and hence mRNA levels shift accordingly.

In still another embodiment of this disclosure, expression levels of proteins listed in SEQ ID NOs 23-44, which correspond to the genes indicated in SEQ ID NOs 1-22, are disclosed. The term "polypeptide" or

"polypeptides" is used interchangeably with the term "protein" or "proteins" herein. As discussed previously, proteins have been long investigated for their potential as biomarkers, with limited success. There is value in protein biomarkers as complementary to polynucleotide biomarkers. Reasons for having the information provided by both types of biomarkers include the current observations that mRNA expression levels are not good predictors of protein expression levels, and that mRNA expression levels tell nothing of the post-translational modifications of proteins that are key to their biological activity. Therefore, in order to understand the expression levels of proteins, and their complete structure, the direct analysis of proteins is required.

FIGS 2A-2B show an exemplary panel of biomarkers from the list of 22 biomarkers for which gene expression levels are compared in the mouse MIN model, and in human subjects. The selection for the panel is taken from across the list of the 22 biomarkers and is taken for the purpose of easy visual assimilation of data in order to demonstrate the utility of a panel. Typically, for complex data sets represented in the 22 member panel of biomarkers, multivariate analysis (MANOVA) is applied, such as that demonstrated in **FIG 2C**.

In **FIG 2A**, the data reported for the mouse MIN studies represent statistical averaging of a number of animal subjects, and the standard error is reported. The p value on the right indicates the degree of confidence that the values are significantly different. As an example, the first gene listed, SDF-1, is related to the human IL-8 gene, and is in the same super family. For SDF-1, the p value of 0.003 indicates that the probability that the differences in the values of the wildtype control and that of the adenomous polyps of the MIN mice occurred by chance alone is only 3 in 1000. Screening the expression levels in adenomous polyps in the subject mice was specifically targeted, since it has been established that adenomous polyps are useful in risk assessment for CRC. What is demonstrated in **FIG**

2A is that the panel of 6 clearly differentiate the results of the MIN mice over that of the wildtype control.

FIGS 2B-2C address the issue of selectivity for biomarker panels. Regarding biomarkers that have an acceptable level of selectivity for CRC, the incidence of CRC for individuals in families with a history of CRC is 3-4 times that of the general population. However, It is now estimated that 6% of all Americans will develop CRC, and of those 70-80% will occur in people of average risk. There is clearly a need for biomarkers that have the necessary selectivity required for confidence in the determination of CRC.

In **FIG 2B**, the same panel of 6 biomarkers established in the mouse MIN model in **FIG 2A** are the basis for determination of CRC in human subjects. In **FIG 2B**, the results of biopsy tissue determined to be normal by histological evaluation taken from patients known to have CRC are compared to biopsy tissue from individuals validated as normal controls. It should be noted that histological methodologies are the accepted standard for the identification of a cancerous colonic lesion. There are two aspects of **FIG 2B** to further discuss. First, values for gene expression profiling for patient vs. normal control may vary either up, as in the case of IL 8, or down, as in the case of PPAR-δ. It is the determination of the collective shift for the patient vs. normal control that is significant when using a panel of biomarkers. Second, in glancing through the patient data, sample-to-sample variation can be noted, which is anticipated, given all the patient-to-patient variables. It is clear at a glance that the expression levels for the panel taken as a group distinguish the patient samples overall from the normal control group, even though a value for any one specific biomarker may not in itself distinguish the patient sample from the normal control. For example, the patient designated as H008 has an expression level for PPAR-δ that is not distinct from the normal control. However, at a glance it is clear that the results of the panel for H008 distinguish it from the normal control set. This demonstrates in principle why a validated panel of markers, given the

complexity and variability of biology, enhance the selectivity of a determination vs. a single marker alone.

Fig 2c further serves to emphasize the value of a panel of biomarkers in enhancing the selectivity of a determination between patient vs. normal samples. An example of demonstrating the use of MANOVA for a panel of 9 biomarkers selected from the group of 22 is demonstrated in **FIG 2C**. In this study, 78 sigmoidal-rectal biopsies from 12 normal patients, and 63 sigmoidal-rectal biopsies from non-cancerous sections of 6 patients with sigmoidal-rectal carcinoma were compared. The Wilks' Lambda criterion was used to assess the difference between the patient samples and normal control samples using the 9 biomarkers listed. The lambda value close to 1.0 signifies a significant difference between the patient and normal samples is indicated, with the probability of about 9 chances in 1000 that the difference is by chance alone.

FIGS 3A-3C and **FIGS 4A-4C** address the issue of sensitivity for biomarker panels. As previously mentioned, since survival rates are greatly enhanced with the earliest indication of CRC, biomarkers for risk assessment and early detection of CRC have been long sought. The difference between risk assessment and early detection is the degree of certainty regarding acquiring CRC. Biomarkers that are used for risk assessment confer less than 100% certainty of CRC within a time interval, whereas biomarkers used for early detection confer an almost 100% certainty of the onset of the disease within a specified time interval. Risk factors may be used as surrogate end points for individuals not diagnosed with cancer, providing they there is an established relationship between the surrogate end point and a definitive outcome. An example of an established surrogate end point for CRC is the example of adenomous polyps. What has been established is that the occurrence of adenomous polyps are a necessary, but not sufficient condition for an individual to later develop CRC. This is demonstrated by the fact that 90% percent of all preinvasive

cancerous lesions are adenomous polyps or precursors, but not all individuals with adenomous polyps go on to later develop CRC.

FIGS 3A-3C show graphs of gene expression levels taken for multiple biopsy samples taken from the colon of one exemplary patient diagnosed with CRC. The determination of cancerous lesions, polyps, and adjacent tissues was made by conventional histological methods. The expression levels for three of the panel of biomarkers are shown for the biopsy samples categorized in that fashion. Again, as was demonstrated with the examples given in FIGS 2A-2C, it is evident that the three markers taken together for the cancerous lesions sampled are significantly different than the normal controls, even though one by itself (CXCR2) would not have been differentiating for this patient. What is additionally indicated in this representation is the distinction between the results of the polyp vs. the normal control. Given that polyps are already accepted as surrogate endpoints for CRC, then a determination of the presence of polyps by a validated analytical methodology using a minimally invasive method, such as a swab, or a non-invasive sampling method, such as a stool sample, would also serve as surrogate end point for risk assessment.

FIGS 4A-4C show the results of gene expression levels for three of the biomarkers in biopsy samples taken over a 53 cm region of the colon of a patient with CRC. The irregularly shaped objects represent biopsy samples that were confirmed to be cancerous lesions by histological methodology, while the oval shapes represent samples that were determined to be non-cancerous by histological methodology. Gene expression profiling was done for each of the biopsy samples, as well. The results of the expression profiling, where the legend indicates relative levels in the patient biopsy samples as compared to normal controls, are depicted in FIGS 4A-4C.

The representation of FIGS 4A-4C indicates the distance over which the biomarkers are able to distinguish differences in the colon tissue for the patient, where these biopsy samples were rendered normal by conventional

histological analysis. These results demonstrate that it is possible to sample cells through a minimally invasive swabbing collection method from an area distant from a cancerous lesion, but capable of indicating a non-normal colon condition. Moreover, collection of a stool sample is an already validated sampling method for collecting sloughed cells or cell debris from which these determinations may be made. In that regard, samples taken either minimally invasively or non-invasively would render samples that could be analyzed using the disclosed panel of biomarkers. Such non-invasive procedures not only reduce the cost of determination of CRC, but reduce the discomfort and risk associated with current methodology. All these factors together increase the attractiveness of regular testing, and hence patient compliance. Increased patient compliance, coupled with an effective determination for CRC, enhance the prospects for early detection, and enhanced survival rates.

Methods and kits for the polynucleotide and polypeptide expression profiling for the panel of molecular markers are also contemplated as part of the present disclosure.

In one embodiment, a method for gene expression profiling comprises measuring cDNA levels for biomarkers selected in the claimed panel. Such a method requires the use of primers, enzymes, and other reagents for the preparation, detection, and quantitation of cDNAs. The method of creating cDNA from mRNA in a sample is referred to as the reverse transcriptase polymer chain reaction (RT-PCR). The primers listed in SEQ ID NOs 45-88 are particularly suited for use in gene expression profiling using RT-PCR based on the claimed panel. A series of primers were designed using Primer Express Software (Applied Biosystems, Foster City, CA). Specific candidates were chosen, and then tested to verify that only cDNA was amplified, and not contaminated by genomic DNA. The primers listed in SEQ ID NOs 45-88 were specifically designed, selected, and tested accordingly. In addition to the primers, reagents such as one including a dinucleotide triphosphate

mixture having all four dinucleotide triphosphates (e.g. dATP, dGTP, dCTP, and dTTP), one having the reverse transcriptase enzyme, and one having a thermostable DNA polymerase are required for RT-PCR. Additionally buffers, inhibitors and activators are also required for the RT-PCR process. Once the cDNA has been sufficiently amplified to a specified end point, the cDNA sample must be prepared for detection and quantitation. Though a number of detection schemes are contemplated, as will be discussed in more detail below, one method contemplated for detection of polynucleotides is fluorescence spectroscopy, and therefore chromophores that are suited to fluorescence spectroscopy are desirable for labeling polynucleotides. One example of such a fluorescent label is SYBR Green, though numerous related chromophores exist, and are known in the art.

In another embodiment, a method for protein expression profiling comprises using an antibody panel based on the claimed panel of biomarkers for measuring targeted polypeptide levels from a biological sample. In one embodiment contemplated for the method, the antibodies for the panel are bound to a solid support. The method for protein expression profiling may use a second antibody having specificity to some portion of the bound polypeptide. Such a second antibody may be labeled with molecules useful for detection and quantitation of the bound polypeptides, and therefore in binding to the polypeptide label it for detection and quantitation. Additionally, other reagents are contemplated for labeling the bound polypeptides for detection and quantitation. Such reagents may either directly label the bound polypeptide or, analogous to a second antibody, may be a moiety with specificity for the bound polypeptide having labels. Examples of such moieties include but are not limited to small molecules such as cofactors, substrates, complexing agents, and the like, or large molecules, such as lectins, peptides, olionucleotides, and the like. Such moieties may be either naturally occurring or synthetic.

Examples of detection modes contemplated for the disclosed

methods include, but are not limited to spectroscopic techniques, such as fluorescence and UV-Vis spectroscopy, scintillation counting, and mass spectroscopy. Complementary to these modes of detection, examples of labels for the purpose of detection and quantitation used in these methods include, but are not limited to chromophoric labels, scintillation labels, and mass labels. The expression levels of polynucleotides and polypeptides measured using these methods may be normalized to a control established for the purpose of the targeted determination. These methods are believed useful in providing determinations as the basis of effective management of patient care for CRC. These methods may also be used in the discovery of therapeutic interventions for CRC. Additionally, not only biopsy samples from sigmoidoscopy, colonoscopy, or surgery may be analyzed by these methods, but biological samples from non-invasive or minimally evasive collection methods are indicated for these methods, as well.

It is further contemplated in what is disclosed to provide kits having the reagents and procedures that facilitate the ready implementation of the methods, and provide consistency and quality control thereby.

In one embodiment, a kit for gene expression profiling comprises the reagents and instructions necessary for the gene expression profiling of the claimed panel. Thus, for example, the reagents may include primers, enzymes, and other reagents for the preparation, detection, and quantitation of cDNAs for the claimed panel of biomarkers. As discussed above, the method of creating cDNA from mRNA in a sample is referred to as the reverse transcriptase polymer chain reaction (RT-PCR). The primers listed in SEQ ID NOs 45-88 are particularly suited for use in gene expression profiling using RT-PCR based on the claimed panel. The primers listed in SEQ ID NOs 45-88 were specifically designed, selected, and tested accordingly. In addition to the primers, reagents such as one including a dinucleotide triphosphate mixture having all four dinucleotide triphosphates (e.g. dATP, dGTP, dCTP, and dTTP), one having the reverse transcriptase

enzyme, and one having a thermostable DNA polymerase are required for RT-PCR. Additionally buffers, inhibitors and activators used for the RT-PCR process are suitable reagents for inclusion in the kit embodiment. Once the cDNA has been sufficiently amplified to a specified end point, the cDNA sample must be prepared for detection and quantitation. One method contemplated for detection of polynucleotides is fluorescence spectroscopy, and therefore chromophores that are suited to fluorescence spectroscopy are desirable for labeling polynucleotides and may also be included in reagents of the kit embodiment. Instructions included with the kit embodiment for gene expression profiling preferably teach the user the following steps: to obtain a biological sample; to isolate cellular RNA from the sample; to amplify copies of cDNA from the sample for each biomarker in the panel, and the panel for which the reagents are provided; and to quantify levels of cDNA amplified from the sample. Though tissue samples from a variety of procedures may be used, the instructions for obtaining a biological sample are preferably whereby the user obtains a sample of colorectal cells in a minimally invasive manner, such as by use of a swab or collection of a stool sample. The instructions may also preferably include the step of comparing the cDNA levels quantified to a control.

In another embodiment, a kit for protein expression profiling comprises the reagents and instructions necessary for protein expression profiling of the claimed panel. Thus, in this embodiment, the kit for protein expression profiling includes supplying an antibody panel based on the claimed panel of biomarkers for measuring targeted polypeptide levels from a biological sample. One embodiment contemplated for such a panel includes the antibody panel bound to a solid support. Additionally, the reagents included with the kit for protein expression profiling may use a second antibody having specificity to some portion of the bound polypeptide. Such a second antibody may be labeled with molecules useful for detection and quantitation of the bound polypeptides, and therefore in binding to the

polypeptide label it for detection and quantitation. Additionally, other reagents are contemplated for labeling the bound polypeptides for detection and quantitation. Such reagents may either directly label the bound polypeptide or, analogous to a second antibody, may be a moiety with specificity for the bound polypeptide having labels. Examples of such moieties include but are not limited to small molecules such as cofactors, substrates, complexing agents, and the like, or large molecules, such as lectins, peptides, olionucleotides, and the like. Such moieties may be either naturally occurring or synthetic. Instructions for the protein expression profiling kit preferably teach the user: to obtain a biological sample; to use the antibody panel supplied with the kit for each biomarker in the panel to bind the polypeptides from the sample; and to quantify levels of polypeptides bound from the sample to the antibody panel. Preferably, the kit instructions also include a step of comparing the polypeptide levels to a control. Preferably the biological sample is obtained by a minimally invasive procedure such as use of a swab to through a stool sample.

Additionally, consumable labware required for sample collection, preparation, and analysis may be provided with the kits.

What has been disclosed herein has been provided for the purposes of illustration and description. It is not intended to be exhaustive or to limit what is disclosed to the precise forms described. Many modifications and variations will be apparent to the practitioner skilled in the art. What is disclosed was chosen and described in order to best explain the principles and practical application of the disclosed embodiments of the art described, thereby enabling others skilled in the art to understand the various embodiments and various modifications that are suited to the particular use contemplated. It is intended that the scope of what is disclosed be defined by the following claims and their equivalence.

What Is Claimed:

1. A panel of biomarkers for colorectal cancer and colorectal polyps comprising at least two polynucleotides selected from SEQ ID NOs 1-5.

2. The panel of claim 1, where the panel is selected for analysis of polynucleotide expression levels for colorectal cancer and colorectal polyps.

3. The panel of claim 2, where the polynucleotide expression levels are mRNAs.

4. The panel of claim 2, where the polynucleotide expression levels are cDNAs.

5. The panel of claim 1, where at least one of the polynucleotides is a fragment.

6. The panel of claim 1, where at least one of the polynucleotides is a variant.

7. The panel of claim 1, where the panel is used for the management of patient care in colorectal cancer and colorectal polyps.

8. The panel of claim 7, where the management of patient care includes one or more of risk assessment, early diagnosis, establishing prognosis, monitoring patient treatment, and detecting relapse.

9. The panel of claim 1, where the panel is used in discovery of therapeutic intervention of colorectal cancer and colorectal polyps.

10. A panel of biomarkers for colorectal cancer and colorectal polyps comprising:

at least two polynucleotides selected from SEQ ID NOs 1-5; and

at least one polynucleotide selected from SEQ ID NOs 6-14

11. The panel of claim 10, where the panel is selected for analysis of polynucleotide expression levels for colorectal cancer and colorectal polyps.

12. The panel of claim 11, where the polynucleotide expression levels are mRNAs.

13. The panel of claim 11, where the polynucleotide expression levels are cDNAs.

14. The panel of claim 10, where at least one of the polynucleotides is a fragment.

15. The panel of claim 10, where at least one of the polynucleotides is a variant.

16. The panel of claim 10, where the panel is used in the management of patient care for colorectal cancer and colorectal polyps.

17. The panel of claim 16, where the management of patient care includes one or more of risk assessment, early diagnosis, establishing prognosis, monitoring patient treatment, and detecting relapse.

18. The panel of claim 10, where the panel is used in discovery of therapeutic intervention of colorectal cancer and colorectal polyps.

19. A panel of biomarkers for colorectal cancer and colorectal polyps comprising:

at least two polynucleotides selected from SEQ ID NOs 1-5;

at least one polynucleotide selected from SEQ ID NOs 6-14; and

at least one polynucleotide selected from SEQ ID NOs 15-22.

20. The panel of claim 19, where the panel is selected for analysis of polynucleotide expression levels for colorectal cancer and colorectal polyps.

21. The panel of claim 20, where the polynucleotide expression levels are mRNAs.

22. The panel of claim 20, where the polynucleotide expression levels are cDNAs.

23. The panel of claim 19, where at least one of the polynucleotides is a fragment.

24. The panel of claim 19, where at least one of the polynucleotides is a variant.

25. The panel of claim 25, where the panel is the basis for management of patient care in colorectal cancer and colorectal polyps.

26. The panel of claim 19, where the management of patient care includes one or more of risk assessment, early diagnosis, establishing prognosis, monitoring patient treatment, and detecting relapse.

27. The panel of claim 25, where the panel is used in discovery of therapeutic intervention of colorectal cancer and colorectal polyps.

28. A panel of biomarkers for colorectal cancer and colorectal polyps comprising at least two polypeptides selected from SEQ ID NOs 23-27.

29. The panel of claim 28, where the panel is selected for analysis of polypeptide expression levels for colorectal cancer and colorectal polyps.

30. The panel of claim 28, where at least one of the polypeptides is a fragment.

31. The panel of claim 28, where at least one of the polypeptides is a variant.

32. The panel of claim 28, where the panel is used in the management of patient care in colorectal cancer and colorectal polyps.

33. The panel of claim 32, where the management of patient care includes one or more of risk assessment, early diagnosis, establishing prognosis, monitoring patient treatment, and detecting relapse.

34. The panel of claim 28, where the panel is used in discovery of therapeutic intervention of colorectal cancer and colorectal polyps.

35. A panel of biomarkers for colorectal cancer and colorectal polyps comprising:

at least two polypeptides selected from SEQ ID NOs 23-27; and

at least one polypeptide selected from SEQ ID NOs 28-36.

36. The panel of claim 35, where the panel is selected for analysis of polypeptide expression levels for colorectal cancer and colorectal polyps.

37. The panel of claim 35, where at least one of the polypeptides is a fragment.

38. The panel of claim 35, where at least one of the polypeptides is a variant.

39. The panel of claim 35, where the panel is used in the management of patient care in colorectal cancer and colorectal polyps.

40. The panel of claim 39, where the management of patient care includes one or more of risk assessment, early diagnosis, establishing prognosis, monitoring patient treatment, and detecting relapse.

41. The panel of claim 35, where the panel is used in discovery of therapeutic intervention of colorectal cancer and colorectal polyps.

42. A panel of biomarkers for colorectal cancer and colorectal polyps comprising:

at least two polypeptides selected from SEQ ID NOs 23-27;
at least one polypeptide selected from SEQ ID NOs 28-36; and
at least one polypeptide selected from SEQ ID NOs 37-44.

43. The panel of claim 42, where the panel is selected for analysis of polypeptide expression levels for colorectal cancer and colorectal polyps.

44. The panel of claim 42, where at least one of the polypeptides is a fragment.

45. The panel of claim 42, where at least one of the polypeptides is a variant.

46. The panel of claim 42, where the panel is used in the management of patient care in colorectal cancer and colorectal polyps.

47. The panel of claim 46, where the management of patient care includes one or more of risk assessment, early diagnosis, establishing prognosis, monitoring patient treatment, and detecting relapse.

48. The panel of claim 42, where the panel is used in discovery of therapeutic intervention of colorectal cancer and colorectal polyps.

49. A method for measuring expression levels of polynucleotides from biomarkers for colorectal cancer and colorectal polyps, comprising:

selecting a panel of biomarkers comprising at least two polynucleotides from SEQ ID NOs 1-5;

obtaining a biological sample;

isolating cellular RNA from the sample;

amplifying copies of cDNA from the sample for each biomarker in the panel; and

quantifying levels of cDNA amplified from the sample.

50. The method of claim 49, where the step of selecting a panel of biomarkers further comprises at least one polynucleotide from SEQ ID NOs 6-14.

51. The method of claim 49, where the step of selecting a panel of biomarkers further comprises:

at least one polynucleotide from SEQ ID NOs 6-14; and

at least one polynucleotide from SEQ ID NOs 15-22.

52. The method of claim 49, where the step of amplifying copies of cDNA further comprises at least two sets of primers chosen from SEQ. ID NOs 45-50.

53. The method of claim 52, where the step of amplifying copies of cDNA further comprises using enzymes and reagents for the preparation of cDNAs.

54. The method of claim 49, where the step of quantifying the levels of cDNA further comprises labeling cDNA.

55. The method of claim 54, where labeling cDNA includes at least one chromophore.

56. The method of claim 49, where the cDNA levels for the sample are compared to a control.

57. The method of claim 56, where the comparison is used in the management of patient care in colorectal cancer and colorectal polyps.

58. The method of claim 57, where the management of patient care includes one or more of risk assessment, early diagnosis, establishing prognosis, monitoring patient treatment, and detecting relapse.

59. The method of claim 56, where the comparison is used in discovery of therapeutic intervention of colorectal cancer and colorectal polyps.

60. The method of claim 49, where the step of obtaining a biological sample is by obtaining a sample of colorectal cells.

61. The method of claim 60, where the step of obtaining a sample of colorectal cells is minimally invasive.

62. The method of claim 61, where the minimally invasive step is by use of a swab.

63. The method of claim 60, where the step of obtaining a sample of colorectal cells is non-invasive.

64. The method of claim 63, where the non-invasive step is by collection of a stool sample.

65. A method for measuring expression levels of polypeptides from biomarkers for colorectal cancer and colorectal cancer, comprising:

selecting a panel of biomarkers comprising at least two polypeptides from SEQ ID NOs 23-27;

obtaining a biological sample;

creating an antibody panel for each biomarker in the panel;

using the antibody panel to bind the polypeptides from the sample; and

quantifying levels of polypeptides bound from the sample to the antibody panel.

66. The method of claim 65, where the step of selecting a panel of biomarkers further comprises at least one polypeptide from SEQ ID NOs 28-36.

67. The method of claim 65, where the step of selecting a panel of biomarkers further comprises:

at least one polypeptide from SEQ ID NOs 28-36; and

at least one polypeptide from SEQ ID NOs 37-44.

68. The method of claim 65, where the polypeptide levels for the sample are compared to a control.

69. The method of claim 68, where the comparison is used in the management of patient care in colorectal cancer and colorectal polyps.

70. The method of claim 69, where the management of patient care includes one or more of risk assessment, early diagnosis, establishing prognosis, monitoring patient treatment, and detecting relapse.

71. The method of claim 68, where the comparison is used in discovery of therapeutic intervention of colorectal cancer and colorectal polyps.

72. The method of claim 65, where the step of obtaining a biological sample is by obtaining a sample of colorectal cells.

73. The method of claim 72, where the step of obtaining a sample of colorectal cells is minimally invasive.

74. The method of claim 73, where the minimally invasive step is by use of a swab.

75. The method of claim 72, where the step of obtaining a sample of colorectal cells is non-invasive.

76. The method of claim 75, where the non-invasive step is by collection of a stool sample.

77. The method of claim 65, where the step of quantifying the bound polypeptides further comprises labeling the polypeptides.

78. The method of claim 77, where labeling the polypeptides comprises using a second antibody.

79. A kit for the determination of colorectal cancer and colorectal polyps comprising:

at least one reagent that is used in analysis of polynucleotide expression levels for a panel of biomarkers for colorectal cancer and colorectal polyps, where the panel comprises at least two polynucleotides listed in SEQ ID NOs 1-5; and

instructions for using the kit for analyzing the expression levels.

80. The kit of claim 79, where the panel of biomarkers further comprises at least one polynucleotides listed in SEQ ID NOs 6-14.

81. The kit of claim 79, where the panel of biomarkers further comprises:

at least one polynucleotide selected from SEQ ID NOs 6-14; and

at least one polynucleotide selected from SEQ ID NOs 15-22.

82. The kit of claim 79, where the polynucleotide expression levels are mRNAs.

83. The kit of claim 79, where the polynucleotide expression levels are cDNAs.

84. The kit of claim 83, where the reagent comprises at least two sets of primers chosen from SEQ. ID NOs 45-50.

85. The kit of claim 84, further comprising reagents for the preparation of cDNA.

86. The kit of claim 79, comprising a reagent that is used for detection and quantitation of polynucleotides.

87. The kit of claim 86, where the reagent includes at least one chromophore.

88. The kit of claim 79, further comprising consumable labware for at least one of sample collection, sample preparation, and sample analysis.

89. A kit for the determination of colorectal cancer and colorectal polyps comprising:

at least one reagent used in that analysis of polypeptide expression levels for a panel of biomarkers for colorectal cancer and colorectal polyps, where the panel comprises at least two polypeptides listed in SEQ. ID NOs 23-27; and

instructions for using the kit for analyzing the expression levels.

90. The kit of claim 89, where the panel of biomarkers further comprises at least one polynucleotides listed in SEQ ID NOs 28-36.

91. The kit of claim 89, where the panel of biomarkers further comprises:
at least one polynucleotide selected from SEQ ID NOs 28-36; and
at least one polynucleotide selected from SEQ ID NOs 37-44.

92. The kit of claim 89, where the reagent is an antibody reagent that binds a polypeptide selected in the panel.

93. The kit of claim 89, further comprising a reagent that is used for detection and quantitation of a bound polypeptide.

94. The kit of claim 93, where the reagent includes a second antibody.

95. The kit of claim 89, further comprising consumable labware for at least one of sample collection, sample preparation, and sample analysis.

Sequence ID No. / ID	NCBI Entrez Database	Name	Abbreviation
1. Coding sequence	XM_031289	Interleukin 8	IL8
2. Coding sequence	XM_051900	Prostaglandin-endoperoxide synthase 2	PTGS2
3. Coding sequence	M94582	Interleukin 8 receptor B	ILR8RB
4. Coding sequence	NM_005555	Lipocalin 2	LCN2
5. Coding sequence	NM_000331	Serum amyloid A1	SAA1
6. Coding sequence	NM_000757	Macrophage colony stimulating factor 1	CSF1 (MCSF1)
7. Coding sequence	X54489	Melanoma growth stimulatory activity	MGSA
8. Coding sequence	NM_002090	Chemokine (C-X-C motif) ligand 3	CXCL3
9. Coding sequence	XM_032429	Secreted phosphoprotein 1	SPP1 (OPN)
10. Coding sequence	M64349	Cyclin D	CCND1
11. Coding sequence	AX057136	c-Myc	c-Myc
12. Coding sequence	L25610	Cyclin-dependent kinase inhibitor	HUMCDK1
13. Coding sequence	BC021998	Cyclin-dependent kinase inhibitor 2A	CDKN2A
14. Coding sequence	NM_058195	Alternative reading frame p14	CDKN2A
15. Coding sequence	NM_005036	Peroxisome proliferative activated receptor, alpha	PPARA
16. Coding sequence	XM_003059	Peroxisome proliferative activated receptor, gamma	PPARG
17. Coding sequence	NM_006238	Peroxisome proliferative activated receptor, delta	PPARD
18. Coding sequence	XM_030326	CD44 antigen	CD44
19. Coding sequence	XM_044882	Prostaglandin-endoperoxide synthase 1	PTGS1
20. Coding sequence	NM_002131	High-mobility group AT-hook1 isoform B	HMGA1
21. Coding sequence	X54942	CKSHS2	CKSHS2
22. Coding sequence	U22055	100 kDa coactivator	p100 coactivator
23. Protein	XP_031289	Interleukin 8	IL8
24. Protein	XP_051900	Prostaglandin-endoperoxide synthase 2	COX2
25. Protein	AAA36108	Interleukin 8 receptor B	CXCR2
26. Protein	NP_005555	Lipocalin 2	LCN2
27. Protein	NP_000331	Serum amyloid A1	SAA1
28. Protein	NP_000757	Macrophage colony stimulating factor 1	MCSF1
29. Protein	CAA38361	Melanoma growth stimulatory activity	Groα
30. Protein	NM-002090	Chemokine (C-X-C motif) ligand 3	Groγ

Figure 1

Sequence ID No. / ID	NCBI Entrez Database	Name	Abbreviation
31. Protein	XP_032429	Osteopontin	OPN
32. Protein	AAA52136	Cyclin D	cyclin D1
33. Protein	CAC22425	c-Myc	c-Myc
34. Protein	AAA16109	Cyclin-dependent kinase inhibitor	p21
35. Protein	AAH21998	Cyclin-dependent kinase inhibitor 2A	p16
36. Protein	NP_047862	Alternative reading frame p14	p14ARF
37. Protein	NP_005027	Peroxisome proliferatie activated receptor, alpha	PPARα
38. Protein	XP_003059	Peroxisome proliferatie activated receptor, gamma	PPARγ
39. Protein	NP_006229	Peroxisome proliferatie activated receptor, delta	PPARδ
40. Protein	XP_030326	CD44 antigen	CD44
41. Protein	XP_044882	Prostaglandin-endoperoxide synthase 1	COX1
42. Protein	NP_002122	High-mobility group AT-hook1 isoform B	HYGYI
43. Protein	CAA38703	CKS1 protein homolog	CKS1
44. Protein	AAA80488	100 kDa coactivator	p100 coactivator
45. Forward primer		Interleukin 8	IL8
46. Reverse primer			
47. Forward primer		Prostaglandin-endoperoxide synthase 2	PTGS2
48. Reverse primer			
49. Forward primer		Interleukin 8 receptor B	ILR8RB
50. Reverse primer			
51. Forward primer		Lipocalin 2	LCN2
52. Reverse primer			
53. Forward primer		Serum amyloid A1	SAA1
54. Reverse primer			
55. Forward primer		Macrophage colony stimulating factor 1	CSF1 (MCSF1)
56. Reverse primer			
57. Forward primer		Melanoma growth stimulatory activity	MGSA
58. Reverse primer			
59. Forward primer		Chemokine (C-X-C motif) ligand 3	MGSA
60. Reverse primer			

Figure 1 – cont'd

Sequence ID No. / ID	NCBI Entrez Database	Name	Abbreviation
61. Forward primer		Secreted phosphoprotein 1	SPP1 (OPN)
62. Reverse primer			
63. Forward primer		Cyclin D	CCND1
64. Reverse primer			
65. Forward primer		c-Myc	c-Myc
66. Reverse primer			
67. Forward primer		Cyclin-dependent kinase inhibitor	HUMCDK1
68. Reverse primer			
69. Forward primer		Cyclin-dependent kinase inhibitor 2A	CDKN2A
70. Reverse primer			
71. Forward primer		Alternative reading frame p14	CDKN2A
72. Reverse primer			
73. Forward primer		Peroxisome proliferative activated receptor, alpha	PPARα
74. Reverse primer			
75. Forward primer		Peroxisome proliferative activated receptor, ganna	PPARγ
76. Reverse primer			
77. Forward primer		Peroxisome proliferative activated receptor, delta	PPARδ
78. Reverse primer			
79. Forward primer		CD44 antigen	CD44
80. Reverse primer			
81. Forward primer		Prostaglandin-endoperoxide synthase 1	COX1
82. Reverse primer			
83. Forward primer		High-mobility group AT-hook1 isoform B	HMGYI
84. Reverse primer			
85. Forward primer		CKS1 protein homolog	CKS1
86. Reverse primer			
87. Forward primer		100 kDa coactivator	p100 coactivator
88. Reverse primer			

Figure 1 – cont'd

Relative Gene Expression Levels in Colon Polyps (Average ± SE)

No.	Genes	Wild-Type Littermate	Individual Poly	P Value
1	SDF-1	1.23±0.34	11.02±2.45	0.003
2	COX2	1.41±0.25	87.48±16.50	<0.001
3	CXCR2	1.41±0.35	11221±23.76	<0.001
4	OPN	1.62±0.60	463.37±130.49	0.004
5	MCSFI	1.05±0.15	4.26±1.60	0.08
6	PPARδ	1.16±0.27	0.44±0.05	0.04

FIG. 2A

Relative Gene Expressions in Normal-Appearing Mucosa from Colon Cancer

	Sigmoid and Rectum						Ascending Colon			
	NB	H002	H004	H006	H008	H011	NB	H003	H009	H010
IL-8	1.80±0.26	28.91	7.14	6.88	18.35	24.67	1.72±0.35	16.03	4.90	28.26
COX2	1.85±0.29	13.54	10.34	18.23	14.63	1.87	1.74±0.45	25.48	11.98	33.06
CXCR2	1.31±0.14	11.35	6.82	6.85	7.18	100.20	1.26±0.17	10.23	22.62	11.20
OPN	2.11±0.52	10.85	9.84	11.88	21.29	3.41	1.43±0.20	26.83	23.97	64.13
MCSF1	1.69±0.19	4.49	11.88	12.84	7.24	7.98	1.57±0.22	12.40	17.89	14.97
PPAR-δ	1.14±0.07	0.10	0.09	0.12	1.28	0.96	1.16±0.11	0.09	1.10	0.30

FIG. 2B

Dependent Variable: Il-8, M-CSF-1, COX-2, OPN, p21, PPAR-γ, CXCR2, CD44, PPAR-δ

Results for Multivariate Analysis: Wilks Lambda Criterion

Source	Lambda	probability
Cancer	0.989	0.0086

FIG. 2C

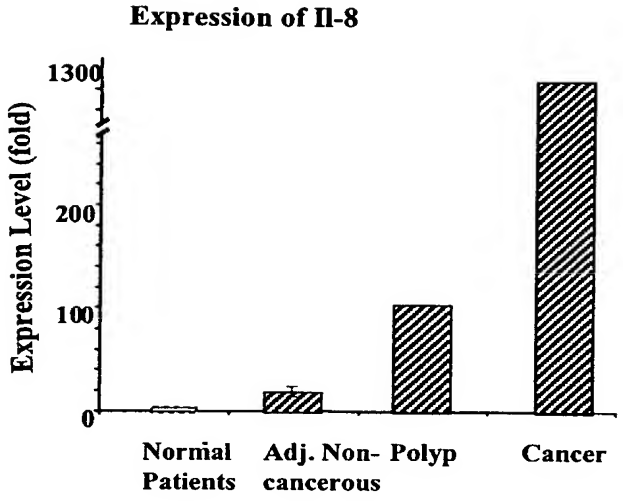

Fig. 3A

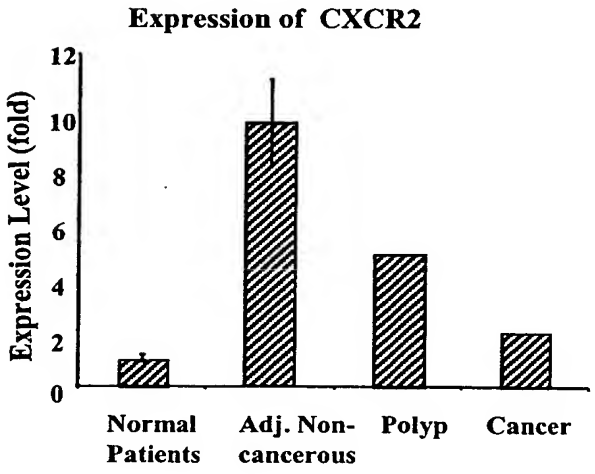

Fig. 3B

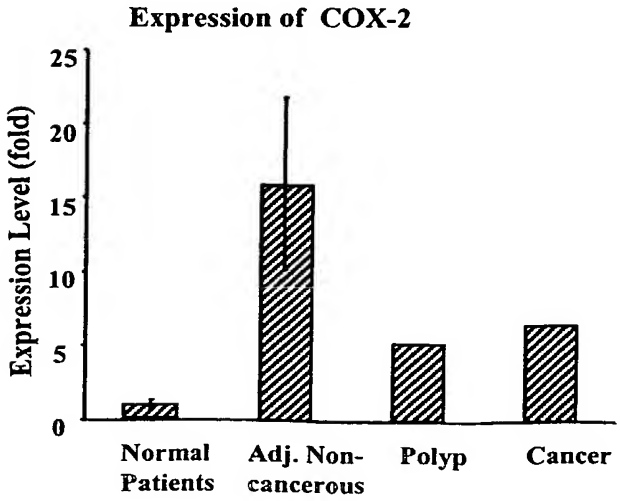

Fig. 3C

IL-8

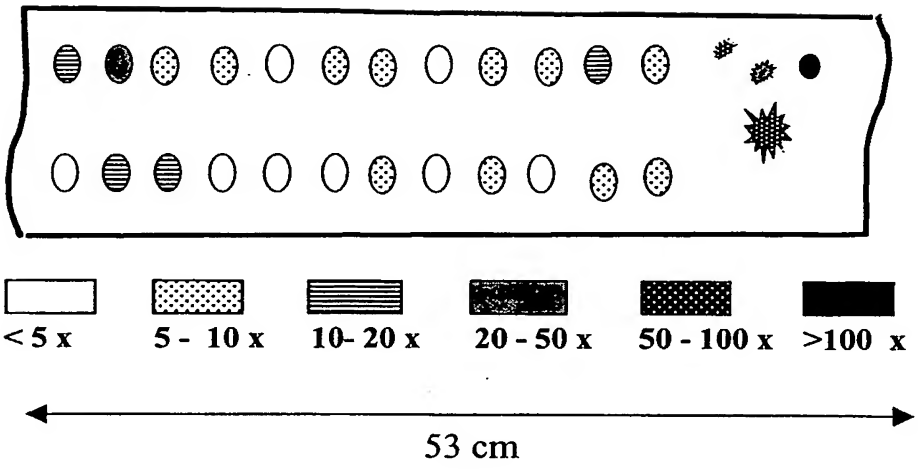

Fig. 4A

COX2

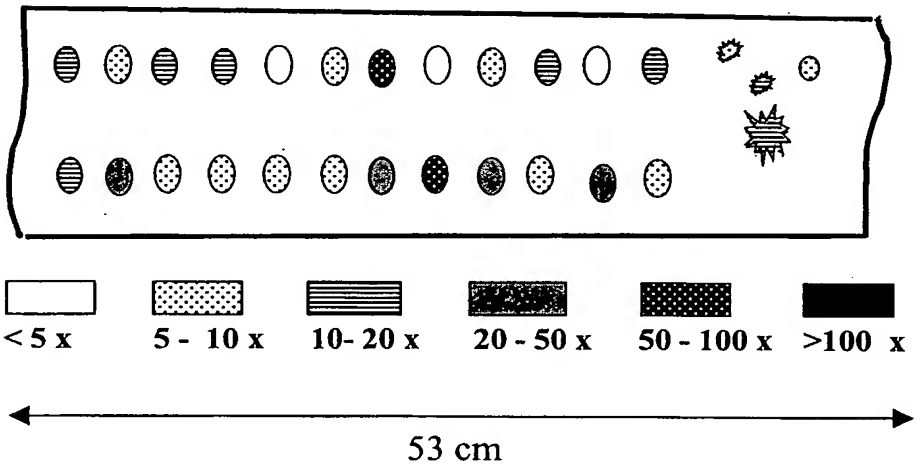

Fig. 4B

CXCR2

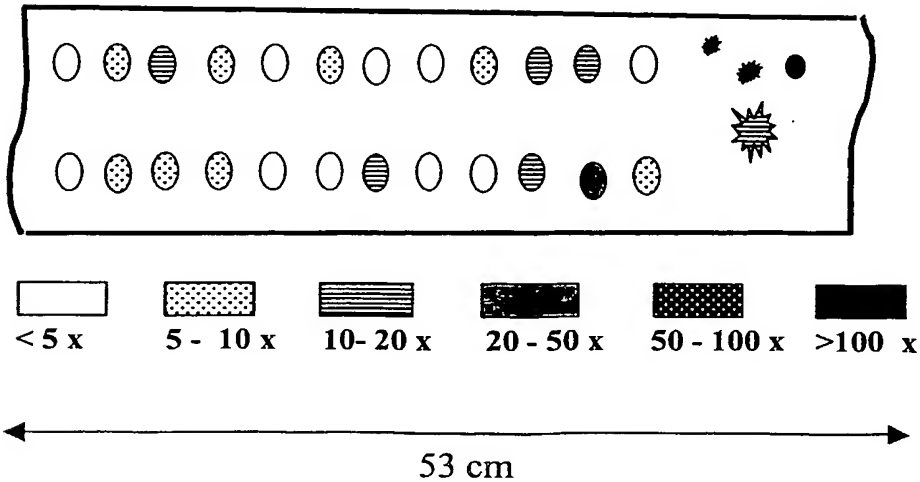

Fig. 4C

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atg tat cct ccc aca gtc aaa gat act cag gca gag atg atc tac cct   883
Met Tyr Pro Pro Thr Val Lys Asp Thr Gln Ala Glu Met Ile Tyr Pro
            250                 255                 260

cct caa gtc cct gag cat cta cgg ttt gct gtg ggg cag gag gtc ttt   931
Pro Gln Val Pro Glu His Leu Arg Phe Ala Val Gly Gln Glu Val Phe
        265                 270                 275

ggt ctg gtg cct ggt ctg atg atg tat gcc aca atc tgg ctg cgg gaa   979
Gly Leu Val Pro Gly Leu Met Met Tyr Ala Thr Ile Trp Leu Arg Glu
    280                 285                 290

cac aac aga gta tgc gat gtg ctt aaa cag gag cat cct gaa tgg ggt   1027
His Asn Arg Val Cys Asp Val Leu Lys Gln Glu His Pro Glu Trp Gly
295                 300                 305                 310

gat gag cag ttg ttc cag aca agc agg cta ata ctg ata gga gag act   1075
Asp Glu Gln Leu Phe Gln Thr Ser Arg Leu Ile Leu Ile Gly Glu Thr
                315                 320                 325

att aag att gtg att gaa gat tat gtg caa cac ttg agt ggc tat cac   1123
Ile Lys Ile Val Ile Glu Asp Tyr Val Gln His Leu Ser Gly Tyr His
            330                 335                 340

ttc aaa ctg aaa ttt gac cca gaa cta ctt ttc aac aaa caa ttc cag   1171
Phe Lys Leu Lys Phe Asp Pro Glu Leu Leu Phe Asn Lys Gln Phe Gln
        345                 350                 355

tac caa aat cgt att gct gct gaa ttt aac acc ctc tat cac tgg cat   1219
Tyr Gln Asn Arg Ile Ala Ala Glu Phe Asn Thr Leu Tyr His Trp His
    360                 365                 370

ccc ctt ctg cct gac acc ttt caa att cat gac cag aaa tac aac tat   1267
Pro Leu Leu Pro Asp Thr Phe Gln Ile His Asp Gln Lys Tyr Asn Tyr
375                 380                 385                 390

caa cag ttt atc tac aac aac tct ata ttg ctg gaa cat gga att acc   1315
Gln Gln Phe Ile Tyr Asn Asn Ser Ile Leu Leu Glu His Gly Ile Thr
                395                 400                 405

cag ttt gtt gaa tca ttc acc agg caa att gct ggc agg gtt gct ggt   1363
Gln Phe Val Glu Ser Phe Thr Arg Gln Ile Ala Gly Arg Val Ala Gly
            410                 415                 420

ggt agg aat gtt cca ccc gca gta cag aaa gta tca cag gct tcc att   1411
Gly Arg Asn Val Pro Pro Ala Val Gln Lys Val Ser Gln Ala Ser Ile
        425                 430                 435

gac cag agc agg cag atg aaa tac cag tct ttt aat gag tac cgc aaa   1459
Asp Gln Ser Arg Gln Met Lys Tyr Gln Ser Phe Asn Glu Tyr Arg Lys
    440                 445                 450
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cgc ttt atg ctg aag ccc tat gaa tca ttt gaa gaa ctt aca gga gaa   1507
Arg Phe Met Leu Lys Pro Tyr Glu Ser Phe Glu Glu Leu Thr Gly Glu
455                 460                 465                 470

aag gaa atg tct gca gag ttg gaa gca ctc tat ggt gac atc gat gct   1555
Lys Glu Met Ser Ala Glu Leu Glu Ala Leu Tyr Gly Asp Ile Asp Ala
                475                 480                 485

gtg gag ctg tat cct gcc ctt ctg gta gaa aag cct cgg cca gat gcc   1603
Val Glu Leu Tyr Pro Ala Leu Leu Val Glu Lys Pro Arg Pro Asp Ala
            490                 495                 500

atc ttt ggt gaa acc atg gta gaa gtt gga gca cca ttc tcc ttg aaa   1651
Ile Phe Gly Glu Thr Met Val Glu Val Gly Ala Pro Phe Ser Leu Lys
        505                 510                 515

gga ctt atg ggt aat gtt ata tgt tct cct gcc tac tgg aag cca agc   1699
Gly Leu Met Gly Asn Val Ile Cys Ser Pro Ala Tyr Trp Lys Pro Ser
    520                 525                 530

act ttt ggt gga gaa gtg ggt ttt caa atc atc aac act gcc tca att   1747
Thr Phe Gly Gly Glu Val Gly Phe Gln Ile Ile Asn Thr Ala Ser Ile
535                 540                 545                 550

cag tct ctc atc tgc aat aac gtg aag ggc tgt ccc ttt act tca ttc   1795
Gln Ser Leu Ile Cys Asn Asn Val Lys Gly Cys Pro Phe Thr Ser Phe
                555                 560                 565

agt gtt cca gat cca gag ctc att aaa aca gtc acc atc aat gca agt   1843
Ser Val Pro Asp Pro Glu Leu Ile Lys Thr Val Thr Ile Asn Ala Ser
            570                 575                 580

tct tcc cgc tcc gga cta gat gat atc aat ccc aca gta cta cta aaa   1891
Ser Ser Arg Ser Gly Leu Asp Asp Ile Asn Pro Thr Val Leu Leu Lys
        585                 590                 595

gaa cgt tcg act gaa ctg tagaagtcta atgatcatat ttatttattt          1939
Glu Arg Ser Thr Glu Leu
    600

atatgaacca tgtctattaa tttaattatt taataatatt tatattaaac tccttatgtt 1999

acttaacatc ttctgtaaca gaagtcagta ctcctgttgc ggagaaagga gtcatacttg 2059

tgaagacttt tatgtcacta ctctaaagat tttgctgttg ctgttaagtt tggaaaacag 2119

tttttattct gttttataaa ccagagagaa atgagttttg acgtcttttt acttgaattt 2179

caacttatat tataagaacg aaagtaaaga tgtttgaata cttaaacact gtcacaagat 2239

ggcaaaatgc tgaaagtttt tacactgtcg atgtttccaa tgcatcttcc atgatgcatt 2299

agaagtaact aatgtttgaa attttaaagt acttttggtt atttttctgt catcaaacaa 2359

aaacaggtat cagtgcatta ttaaatgaat atttaaatta gacattacca gtaatttcat 2419

gtctactttt taaaatcagc aatgaaacaa taatttgaaa tttctaaatt catagggtag 2479
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aatcacctgt aaaagcttgt ttgatttctt aaagttatta aacttgtaca tataccaaaa 2539

agaagctgtc ttggatttaa atctgtaaaa tcagtagaaa ttttactaca attgcttgtt 2599

aaaatatttt ataagtgatg ttccttttc accaagagta taaacctttt tagtgtgact 2659

gttaaaactt ccttttaaat caaaatgcca aatttattaa ggtggtggag ccactgcagt 2719

gttatcttaa aataagaata ttttgttgag atattccaga atttgtttat atggctggta 2779

acatgtaaaa tctatatcag caaaagggtc tacctttaaa ataagcaata acaaagaaga 2839

aaaccaaatt attgttcaaa tttaggttta aacttttgaa gcaaactttt ttttatcctt 2899

gtgcactgca ggcctggtac tcagattttg ctatgaggtt aatgaagtac caagctgtgc 2959

ttgaataatg atatgttttc tcagattttc tgttgtacag tttaatttag cagtccatat 3019

cacattgcaa aagtagcaat gacctcataa aatacctctt caaaatgctt aaattcattt 3079

cacacattaa ttttatctca gtcttgaagc caattcagta ggtgcattgg aatcaagcct 3139

ggctacctgc atgctgttcc ttttcttttc ttcttttagc cattttgcta agagacacag 3199

tcttctcatc acttcgtttc tcctattttg ttttactagt tttaagatca gagttcactt 3259

tctttggact ctgcctatat tttcttacct gaacttttgc aagttttcag gtaaacctca 3319

gctcaggact gctatttagc tcctcttaag aagatta 3356

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<213> Homo sapiens

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<400> 3
cctacaggtg aaaagcccag cgacccagtc aggatttaag tttacctcaa aa atg gaa 58
Met Glu
1

gat ttt aac atg gag agt gac agc ttt gaa gat ttc tgg aaa ggt gaa 106
Asp Phe Asn Met Glu Ser Asp Ser Phe Glu Asp Phe Trp Lys Gly Glu
5 10 15

gat ctt agt aat tac agt tac agc tct acc ctg ccc cct ttt cta cta 154
Asp Leu Ser Asn Tyr Ser Tyr Ser Ser Thr Leu Pro Pro Phe Leu Leu
20 25 30

gat gcc gcc cca tgt gaa cca gaa tcc ctg gaa atc aac aag tat ttt 202
Asp Ala Ala Pro Cys Glu Pro Glu Ser Leu Glu Ile Asn Lys Tyr Phe
35 40 45 50

```
gtg gtc att atc tat gcc ctg gta ttc ctg ctg agc ctg ctg gga aac   250
Val Val Ile Ile Tyr Ala Leu Val Phe Leu Leu Ser Leu Leu Gly Asn
                 55                  60                  65

tcc ctc gtg atg ctg gtc atc tta tac agc agg gtc ggc cgc tcc gtc   298
Ser Leu Val Met Leu Val Ile Leu Tyr Ser Arg Val Gly Arg Ser Val
             70                  75                  80

act gat gtc tac ctg ctg aac cta gcc ttg gcc gac cta ctc ttt gcc   346
Thr Asp Val Tyr Leu Leu Asn Leu Ala Leu Ala Asp Leu Leu Phe Ala
         85                  90                  95

ctg acc ttg ccc atc tgg gcc gcc tcc aag gtg aat ggc tgg att ttt   394
Leu Thr Leu Pro Ile Trp Ala Ala Ser Lys Val Asn Gly Trp Ile Phe
    100                 105                 110

ggc aca ttc ctg tgc aag gtg gtc tca ctc ctg aag gaa gtc aac ttc   442
Gly Thr Phe Leu Cys Lys Val Val Ser Leu Leu Lys Glu Val Asn Phe
115                 120                 125                 130

tat agt ggc atc ctg cta ctg gcc tgc atc agt gtg gac cgt tac ctg   490
Tyr Ser Gly Ile Leu Leu Leu Ala Cys Ile Ser Val Asp Arg Tyr Leu
                135                 140                 145

gcc att gtc cat gcc aca cgc aca ctg acc cag aag cgc tac ttg gtc   538
Ala Ile Val His Ala Thr Arg Thr Leu Thr Gln Lys Arg Tyr Leu Val
            150                 155                 160

aaa ttc ata tgt ctc agc atc tgg ggt ctg tcc ttg ctc ctg gcc ctg   586
Lys Phe Ile Cys Leu Ser Ile Trp Gly Leu Ser Leu Leu Leu Ala Leu
        165                 170                 175

cct gtc tta ctt ttc cga agg acc gtc tac tca tcc aat gtt agc cca   634
Pro Val Leu Leu Phe Arg Arg Thr Val Tyr Ser Ser Asn Val Ser Pro
    180                 185                 190

gcc tgc tat gag gac atg ggc aac aat aca gca aac tgg cgg atg ctg   682
Ala Cys Tyr Glu Asp Met Gly Asn Asn Thr Ala Asn Trp Arg Met Leu
195                 200                 205                 210

tta cgg atc ctg ccc cag tcc ttt ggc ttc atc gtg cca ctg ctg atc   730
Leu Arg Ile Leu Pro Gln Ser Phe Gly Phe Ile Val Pro Leu Leu Ile
                215                 220                 225

atg ctg ttc tgc tac gga ttc acc ctg cgt acg ctg ttt aag gcc cac   778
Met Leu Phe Cys Tyr Gly Phe Thr Leu Arg Thr Leu Phe Lys Ala His
            230                 235                 240

atg ggg cag aag cac cgg gcc atg cgg gtc atc ttt gct gtc gtc ctc   826
Met Gly Gln Lys His Arg Ala Met Arg Val Ile Phe Ala Val Val Leu
        245                 250                 255

atc ttc ctg ctt tgc tgg ctg ccc tac aac ctg gtc ctg ctg gca gac   874
Ile Phe Leu Leu Cys Trp Leu Pro Tyr Asn Leu Val Leu Leu Ala Asp
    260                 265                 270
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acc ctc atg agg acc cag gtg atc cag gag acc tgt gag cgc cgc aat   922
Thr Leu Met Arg Thr Gln Val Ile Gln Glu Thr Cys Glu Arg Arg Asn
275                 280                 285                 290

cac atc gac cgg gct ctg gat gcc acc gag att ctg ggc atc ctt cac   970
His Ile Asp Arg Ala Leu Asp Ala Thr Glu Ile Leu Gly Ile Leu His
                295                 300                 305

agc tgc ctc aac ccc ctc atc tac gcc ttc att ggc cag aag ttt cgc   1018
Ser Cys Leu Asn Pro Leu Ile Tyr Ala Phe Ile Gly Gln Lys Phe Arg
            310                 315                 320

cat gga ctc ctc aag att cta gct ata cat ggc ttg atc agc aag gac   1066
His Gly Leu Leu Lys Ile Leu Ala Ile His Gly Leu Ile Ser Lys Asp
        325                 330                 335

tcc ctg ccc aaa gac agc agg cct tcc ttt gtt ggc tct tct tca ggg   1114
Ser Leu Pro Lys Asp Ser Arg Pro Ser Phe Val Gly Ser Ser Ser Gly
    340                 345                 350

cac act tcc act act ctc taagacctcc tgcctaagtg cagccccgtg          1162
His Thr Ser Thr Thr Leu
355                 360

gggttcctcc cttctcttca cagtcacatt ccaagcctca tgtccactgg ttcttcttgg 1222

tctcagtgtc aatgcagccc ccattgtggt cacaggaagc agaggaggcc acgttcttac 1282

tagtttccct tgcatggttt agaaagcttg ccctggtgcc tcacccctttg ccataattac 1342

tatgtcattt gctggagctc tgcccatcct gcccctgagc ccatggcact ctatgttcta 1402

agaagtgaaa atctacactc cagtgagaca gctctgcata ctcattagga tggctagtat 1462

caaaagaaag aaaatcaggc tggccaacgg gatgaaaccc tgtctctact aaaaatacaa 1522

aaaaaaaaaa aaaaattagc cgggcgtggt ggtgagtgcc tgtaatcaca gctacttggg 1582

aggctgagat gggagaatca cttgaacccg ggaggcagag gttgcagtga gccgagattg 1642

tgcccctgca ctccagcctg agcgacagtg agactctgtc tcagtccatg aagatgtaga 1702

ggagaaactg gaactctcga gcgttgctgg gggggattgt aaaatggt               1750


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<212> DNA
<213> Homo sapiens

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Met Pro Leu Gly Leu Leu Trp Leu Gly Leu Ala Leu Leu Gly Ala Leu
  1               5                  10                  15
```

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cat gcc cag gcc cag gac tcc acc tca gac ctg atc cca gcc cca cct   96
His Ala Gln Ala Gln Asp Ser Thr Ser Asp Leu Ile Pro Ala Pro Pro
             20                  25                  30

ctg agc aag gtc cct ctg cag cag aac ttc cag gac aac caa ttc cag   144
Leu Ser Lys Val Pro Leu Gln Gln Asn Phe Gln Asp Asn Gln Phe Gln
         35                  40                  45

ggg aag tgg tat gtg gta ggc ctg gca ggg aat gca att ctc aga gaa   192
Gly Lys Trp Tyr Val Val Gly Leu Ala Gly Asn Ala Ile Leu Arg Glu
     50                  55                  60

gac aaa gac ccg caa aag atg tat gcc acc atc tat gag ctg aaa gaa   240
Asp Lys Asp Pro Gln Lys Met Tyr Ala Thr Ile Tyr Glu Leu Lys Glu
 65                  70                  75                  80

gac aag agc tac aat gtc acc tcc gtc ctg ttt agg aaa aag aag tgt   288
Asp Lys Ser Tyr Asn Val Thr Ser Val Leu Phe Arg Lys Lys Lys Cys
                 85                  90                  95

gac tac tgg atc agg act ttt gtt cca ggt tgc cag ccc ggc gag ttc   336
Asp Tyr Trp Ile Arg Thr Phe Val Pro Gly Cys Gln Pro Gly Glu Phe
            100                 105                 110

acg ctg ggc aac att aag agt tac cct gga tta acg agt tac ctc gtc   384
Thr Leu Gly Asn Ile Lys Ser Tyr Pro Gly Leu Thr Ser Tyr Leu Val
        115                 120                 125

cga gtg gtg agc acc aac tac aac cag cat gct atg gtg ttc ttc aag   432
Arg Val Val Ser Thr Asn Tyr Asn Gln His Ala Met Val Phe Phe Lys
    130                 135                 140

aaa gtt tct caa aac agg gag tac ttc aag atc acc ctc tac ggg aga   480
Lys Val Ser Gln Asn Arg Glu Tyr Phe Lys Ile Thr Leu Tyr Gly Arg
145                 150                 155                 160

acc aag gag ctg act tcg gaa cta aag gag aac ttc atc cgc ttc tcc   528
Thr Lys Glu Leu Thr Ser Glu Leu Lys Glu Asn Phe Ile Arg Phe Ser
                165                 170                 175

aaa tat ctg ggc ctc cct gaa aac cac atc gtc ttc cct gtc cca atc   576
Lys Tyr Leu Gly Leu Pro Glu Asn His Ile Val Phe Pro Val Pro Ile
            180                 185                 190

gac cag tgt atc gac ggc tga                                     597
Asp Gln Cys Ile Asp Gly
        195
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<211> 369
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> (1)..(369)

<400> 5
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Met Lys Leu Leu Thr Gly Leu Val Phe Cys Ser Leu Val Leu Gly Val
1 5 10 15

agc agc cga agc ttc ttt tcg ttc ctt ggc gag gct ttt gat ggg gct 96
Ser Ser Arg Ser Phe Phe Ser Phe Leu Gly Glu Ala Phe Asp Gly Ala
20 25 30

cgg gac atg tgg aga gcc tac tct gac atg aga gaa gcc aat tac atc 144
Arg Asp Met Trp Arg Ala Tyr Ser Asp Met Arg Glu Ala Asn Tyr Ile
35 40 45

ggc tca gac aaa tac ttc cat gct cgg ggg aac tat gat gct gcc aaa 192
Gly Ser Asp Lys Tyr Phe His Ala Arg Gly Asn Tyr Asp Ala Ala Lys
50 55 60

agg gga cct ggg ggt gtc tgg gct gca gaa gcg atc agc gat gcc aga 240
Arg Gly Pro Gly Gly Val Trp Ala Ala Glu Ala Ile Ser Asp Ala Arg
65 70 75 80

gag aat atc cag aga ttc ttt ggc cat ggt gcg gag gac tcg ctg gct 288
Glu Asn Ile Gln Arg Phe Phe Gly His Gly Ala Glu Asp Ser Leu Ala
85 90 95

gat cag gct gcc aat gaa tgg ggc agg agt ggc aaa gac ccc aat cac 336
Asp Gln Ala Ala Asn Glu Trp Gly Arg Ser Gly Lys Asp Pro Asn His
100 105 110

ttc cga cct gct ggc ctg cct gag aaa tac tga 369
Phe Arg Pro Ala Gly Leu Pro Glu Lys Tyr
115 120

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<222> (106)..(1767)

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cctgggtcct ctcggcgcca gagccgctct ccgcatccca ggacagcggt gcggccctcg 60

gccggggcgc ccactccgca gcagccagcg agccagctgc cccgt atg acc gcg ccg 117
Met Thr Ala Pro
1

ggc gcc gcc ggg cgc tgc cct ccc acg aca tgg ctg ggc tcc ctg ctg 165
Gly Ala Ala Gly Arg Cys Pro Pro Thr Thr Trp Leu Gly Ser Leu Leu
5 10 15 20

```
ttg ttg gtc tgt ctc ctg gcg agc agg agt atc acc gag gag gtg tcg   213
Leu Leu Val Cys Leu Leu Ala Ser Arg Ser Ile Thr Glu Glu Val Ser
                25                  30                  35

gag tac tgt agc cac atg att ggg agt gga cac ctg cag tct ctg cag   261
Glu Tyr Cys Ser His Met Ile Gly Ser Gly His Leu Gln Ser Leu Gln
            40                  45                  50

cgg ctg att gac agt cag atg gag acc tcg tgc caa att aca ttt gag   309
Arg Leu Ile Asp Ser Gln Met Glu Thr Ser Cys Gln Ile Thr Phe Glu
        55                  60                  65

ttt gta gac cag gaa cag ttg aaa gat cca gtg tgc tac ctt aag aag   357
Phe Val Asp Gln Glu Gln Leu Lys Asp Pro Val Cys Tyr Leu Lys Lys
    70                  75                  80

gca ttt ctc ctg gta caa gac ata atg gag gac acc atg cgc ttc aga   405
Ala Phe Leu Leu Val Gln Asp Ile Met Glu Asp Thr Met Arg Phe Arg
85                  90                  95                  100

gat aac acc gcc aat ccc atc gcc att gtg cag ctg cag gaa ctc tct   453
Asp Asn Thr Ala Asn Pro Ile Ala Ile Val Gln Leu Gln Glu Leu Ser
                105                 110                 115

ttg agg ctg aag agc tgc ttc acc aag gat tat gaa gag cat gac aag   501
Leu Arg Leu Lys Ser Cys Phe Thr Lys Asp Tyr Glu Glu His Asp Lys
            120                 125                 130

gcc tgc gtc cga act ttc tat gag aca cct ctc cag ttg ctg gag aag   549
Ala Cys Val Arg Thr Phe Tyr Glu Thr Pro Leu Gln Leu Leu Glu Lys
        135                 140                 145

gtc aag aat gtc ttt aat gaa aca aag aat ctc ctt gac aag gac tgg   597
Val Lys Asn Val Phe Asn Glu Thr Lys Asn Leu Leu Asp Lys Asp Trp
    150                 155                 160

aat att ttc agc aag aac tgc aac aac agc ttt gct gaa tgc tcc agc   645
Asn Ile Phe Ser Lys Asn Cys Asn Asn Ser Phe Ala Glu Cys Ser Ser
165                 170                 175                 180

caa gat gtg gtg acc aag cct gat tgc aac tgc ctg tac ccc aaa gcc   693
Gln Asp Val Val Thr Lys Pro Asp Cys Asn Cys Leu Tyr Pro Lys Ala
                185                 190                 195

atc cct agc agt gac ccg gcc tct gtc tcc cct cat cag ccc ctc gcc   741
Ile Pro Ser Ser Asp Pro Ala Ser Val Ser Pro His Gln Pro Leu Ala
            200                 205                 210

ccc tcc atg gcc cct gtg gct ggc ttg acc tgg gag gac tct gag gga   789
Pro Ser Met Ala Pro Val Ala Gly Leu Thr Trp Glu Asp Ser Glu Gly
        215                 220                 225

act gag ggc agc tcc ctc ttg cct ggt gag cag ccc ctg cac aca gtg   837
Thr Glu Gly Ser Ser Leu Leu Pro Gly Glu Gln Pro Leu His Thr Val
    230                 235                 240
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```
gat cca ggc agt gcc aag cag cgg cca ccc agg agc acc tgc cag agc   885
Asp Pro Gly Ser Ala Lys Gln Arg Pro Pro Arg Ser Thr Cys Gln Ser
245                 250                 255                 260

ttt gag ccg cca gag acc cca gtt gtc aag gac agc acc atc ggt ggc   933
Phe Glu Pro Pro Glu Thr Pro Val Val Lys Asp Ser Thr Ile Gly Gly
                265                 270                 275

tca cca cag cct cgc ccc tct gtc ggg gcc ttc aac ccc ggg atg gag   981
Ser Pro Gln Pro Arg Pro Ser Val Gly Ala Phe Asn Pro Gly Met Glu
            280                 285                 290

gat att ctt gac tct gca atg ggc act aat tgg gtc cca gaa gaa gcc   1029
Asp Ile Leu Asp Ser Ala Met Gly Thr Asn Trp Val Pro Glu Glu Ala
        295                 300                 305

tct gga gag gcc agt gag att ccc gta ccc caa ggg aca gag ctt tcc   1077
Ser Gly Glu Ala Ser Glu Ile Pro Val Pro Gln Gly Thr Glu Leu Ser
    310                 315                 320

ccc tcc agg cca gga ggg ggc agc atg cag aca gag ccc gcc aga ccc   1125
Pro Ser Arg Pro Gly Gly Gly Ser Met Gln Thr Glu Pro Ala Arg Pro
325                 330                 335                 340

agc aac ttc ctc tca gca tct tct cca ctc cct gca tca gca aag ggc   1173
Ser Asn Phe Leu Ser Ala Ser Ser Pro Leu Pro Ala Ser Ala Lys Gly
                345                 350                 355

caa cag ccg gca gat gta act gct aca gcc ttg ccc agg gtg ggc ccc   1221
Gln Gln Pro Ala Asp Val Thr Ala Thr Ala Leu Pro Arg Val Gly Pro
            360                 365                 370

gtg atg ccc act ggc cag gac tgg aat cac acc ccc cag aag aca gac   1269
Val Met Pro Thr Gly Gln Asp Trp Asn His Thr Pro Gln Lys Thr Asp
        375                 380                 385

cat cca tct gcc ctg ctc aga gac ccc ccg gag cca ggc tct ccc agg   1317
His Pro Ser Ala Leu Leu Arg Asp Pro Pro Glu Pro Gly Ser Pro Arg
    390                 395                 400

atc tca tca ctg cgc ccc cag gcc ctc agc aac ccc tcc acc ctc tct   1365
Ile Ser Ser Leu Arg Pro Gln Ala Leu Ser Asn Pro Ser Thr Leu Ser
405                 410                 415                 420

gct cag cca cag ctt tcc aga agc cac tcc tcg ggc agc gtg ctg ccc   1413
Ala Gln Pro Gln Leu Ser Arg Ser His Ser Ser Gly Ser Val Leu Pro
                425                 430                 435

ctt ggg gag ctg gag ggc agg agg agc acc agg gat cgg acg agc ccc   1461
Leu Gly Glu Leu Glu Gly Arg Arg Ser Thr Arg Asp Arg Thr Ser Pro
            440                 445                 450

gca gag cca gaa gca gca cca gca agt gaa ggg gca gcc agg ccc ctg   1509
Ala Glu Pro Glu Ala Ala Pro Ala Ser Glu Gly Ala Ala Arg Pro Leu
        455                 460                 465
```

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ccc cgt ttt aac tcc gtt cct ttg act gac aca ggc cat gag agg cag   1557
Pro Arg Phe Asn Ser Val Pro Leu Thr Asp Thr Gly His Glu Arg Gln
    470                 475                 480

tcc gag gga tcc tcc agc ccg cag ctc cag gag tct gtc ttc cac ctg   1605
Ser Glu Gly Ser Ser Ser Pro Gln Leu Gln Glu Ser Val Phe His Leu
485                 490                 495                 500

ctg gtg ccc agt gtc atc ctg gtc ttg ctg gct gtc gga ggc ctc ttg   1653
Leu Val Pro Ser Val Ile Leu Val Leu Leu Ala Val Gly Gly Leu Leu
                505                 510                 515

ttc tac agg tgg agg cgg cgg agc cat caa gag cct cag aga gcg gat   1701
Phe Tyr Arg Trp Arg Arg Arg Ser His Gln Glu Pro Gln Arg Ala Asp
            520                 525                 530

tct ccc ttg gag caa cca gag ggc agc ccc ctg act cag gat gac aga   1749
Ser Pro Leu Glu Gln Pro Glu Gly Ser Pro Leu Thr Gln Asp Asp Arg
        535                 540                 545

cag gtg gaa ctg cca gtg tagagggaat tctaagctgg acgcacagaa          1797
Gln Val Glu Leu Pro Val
    550

cagtctcttc gtgggaggag acattatggg gcgtccacca ccacccctcc ctggccatcc 1857

tcctggaatg tggtctgccc tccaccagag ctcctgcctg ccaggactgg accagagcag 1917

ccaggctggg gcccctctgt ctcaacccgc agacccttga ctgaatgaga gaggccagag 1977

gatgctcccc atgctgccac tatttattgt gagccctgga ggctcccatg tgcttgagga 2037

aggctggtga gcccggctca ggaccctctt ccctcagggg ctgcagcctc ctctcactcc 2097

cttccatgcc ggaacccagg ccagggaccc accggcctgt ggtttgtggg aaagcagggt 2157

gcacgctgag gagtgaaaca accctgcacc cagagggcct gcctggtgcc aaggtatccc 2217

agcctggaca ggcatggacc tgtctccaga cagaggagcc tgaagttcgt ggggcgggac 2277

agcctcggcc tgatttcccg taaaggtgtg cagcctgaga gacgggaaga ggaggcctct 2337

gcacctgctg gtctgcactg acagcctgaa gggtctacac cctcggctca cctaagtccc 2397

tgtgctggtt gccaggccca gaggggaggc cagccctgcc ctcaggacct gcctgacctg 2457

ccagtgatgc caagaggggg atcaagcact ggcctctgcc cctcctcctt ccagcacctg 2517

ccagagcttc tccagcaggc caagcagagg ctcccctcat gaaggaagcc attgcactgt 2577

gaacactgta cctgcctgct gaacagcctc cccccgtcca tccatgagcc agcatccgtc 2637

cgtcctccac tctccagcct ctccccagcc tcctgcactg agctggcctc accagtcgac 2697

tgagggagcc cctcagccct gaccttctcc tgacctggcc tttgactccc cggagtggag 2757

tggggtggga gaacctcctg ggccgccagc cagagccgct ctttaggctg tgttcttcgc 2817
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ccaggtttct gcatcttcca ctttgacatt cccaagaggg aagggactag tgggagagag 2877

caagggaggg gagggcacag acagagagcc tacagggcga gctctgactg aagatgggcc 2937

tttgaaatat aggtatgcac ctgaggttgg gggagggtct gcactcccaa accccagcgc 2997

agtgtccttt ccctgctgcc gacaggaacc tggggctgag caggttatcc ctgtcaggag 3057

ccctggactg ggctgcatct cagccccacc tgcatggtat ccagctccca tccacttctc 3117

acccttcttt cctcctgacc ttggtcagca gtgatgacct ccaactctca cccacccccct 3177

ctaccatcac ctctaaccag gcaagccagg gtgggagagc aatcaggaga gccaggcctc 3237

agcttccaat gcctggaggg cctccacttt gtggccagcc tgtggtgctg gctctgaggc 3297

ctaggcaacg agcgacaggg ctgccagttg cccctgggtt cctttgtgct gctgtgtgcc 3357

tcctctcctg ccgccctttg tcctccgcta agagaccctg ccctacctgg ccgctgggcc 3417

ccgtgacttt cccttcctgc ccaggaaagt gagggtcggc tggccccacc ttccctgtcc 3477

tgatgccgac agcttaggga agggcactga acttgcatat ggggcttagc cttctagtca 3537

cagcctctat atttgatgct agaaaacaca tatttttaaa tggaagaaaa ataaaaaggc 3597

attccccctt catccccta ccttaaacat ataatatttt aaaggtcaaa aaagcaatcc 3657

aacccactgc agaagctctt tttgagcact tggtggcatc agagcaggag gagccccaga 3717

gccacctctg gtgtccccca ggctacctgc tcaggaaccc cttctgttct ctgagaactc 3777

aacagaggac attggctcac gcactgtgag attttgtttt tatacttgca actggtgaat 3837

tatttttat aaagtcattt aaatatctat ttaaaagata ggaagctgct tatatattta 3897

ataataaaag aagtgcacaa gctgccgttg acgtagctcg ag 3939

<210> 7
<211> 1024
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> (1)..(321)

<400> 7
atg gcc cgc gct gct ctc tcc gcc gcc ccc agc aat ccc cgg ctc ctg 48
Met Ala Arg Ala Ala Leu Ser Ala Ala Pro Ser Asn Pro Arg Leu Leu
1 5 10 15

cga gtg gca ctg ctg ctc ctg ctc ctg gta gcc gct ggc cgg cgc gca 96
Arg Val Ala Leu Leu Leu Leu Leu Leu Val Ala Ala Gly Arg Arg Ala
20 25 30

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gca gga gcg tcc gtg gcc act gaa ctg cgc tgc cag tgc ttg cag acc   144
Ala Gly Ala Ser Val Ala Thr Glu Leu Arg Cys Gln Cys Leu Gln Thr
         35                  40                  45

ctg cag gga att cac ccc aag aac atc caa agt gtg aac gtg aag tcc   192
Leu Gln Gly Ile His Pro Lys Asn Ile Gln Ser Val Asn Val Lys Ser
     50                  55                  60

ccc gga ccc cac tgc gcc caa acc gaa gtc ata gcc aca ctc aag aat   240
Pro Gly Pro His Cys Ala Gln Thr Glu Val Ile Ala Thr Leu Lys Asn
 65                  70                  75                  80

ggg cgg aaa gct tgc ctc aat cct gca tcc ccc ata gtt aag aaa atc   288
Gly Arg Lys Ala Cys Leu Asn Pro Ala Ser Pro Ile Val Lys Lys Ile
                 85                  90                  95

atc gaa aag atg ctg aac agt gac aaa tcc aac tgaccagaag ggaggaggaa 341
Ile Glu Lys Met Leu Asn Ser Asp Lys Ser Asn
            100                 105

gctcactggt ggctgttcct gaaggaggcc ctgcccttat aggaacagaa gaggaaagag 401

agacacagct gcagaggcca cctggattgt gcctaatgtg tttgagcatc gcttaggaga 461

agtcttctat ttatttattt attcattagt tttgaagatt ctatgttaat attttaggtg 521

taaaataatt aagggtatga ttaactctac ctgcacactg tcctattata ttcattcttt 581

ttgaaatgtc aaccccaagt tagttcaatc tggattcata tttaatttga aggtagaatg 641

ttttcaaatg ttctccagtc attatgttaa tatttctgag gagcctgcaa catgccagcc 701

actgtgatag aggctggcgg atccaagcaa atggccaatg agatcattgt gaaggcaggg 761

gaatgtatgt gcacatctgt tttgtaactg tttagatgaa tgtcagttgt tatttattga 821

aatgatttca cagtgtgtgg tcaacatttc tcatgttgaa actttaagaa ctaaaatgtt 881

ctaaatatcc cttggacatt ttatgtcttt cttgtaaggc atactgcctt gtttaatggt 941

agttttacag tgtttctggc ttagaacaaa ggggcttaat tattgatgtt ttcatagaga 1001

atataaaaat aaagcactta tag                                        1024
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<210> 8
<211> 1064
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> (78)..(395)

<220>
<221> modified_base

<222> (27)
<223> a, c, t, g, other or unknown

<220>
<221> modified_base
<222> (766)
<223> a, c, t, g, other or unknown

<400> 8
cacagccggg tcgcaggcac ctccccngcc agctctcccg cattctgcac agcttcccga 60

cgcgtctgct gagcccc atg gcc cac gcc acg ctc tcc gcc gcc ccc agc 110
Met Ala His Ala Thr Leu Ser Ala Ala Pro Ser
1 5 10

aat ccc cgg ctc ctg cgg gtg gcg ctg ctg ctc ctg ctc ctg gtg ggc 158
Asn Pro Arg Leu Leu Arg Val Ala Leu Leu Leu Leu Leu Leu Val Gly
15 20 25

agc cgg cgc gca gca gga gcg tcc gtg gtc act gaa ctg cgc tgc cag 206
Ser Arg Arg Ala Ala Gly Ala Ser Val Val Thr Glu Leu Arg Cys Gln
30 35 40

tgc ttg cag aca ctg cag gga att cac ctc aag aac atc caa agt gtg 254
Cys Leu Gln Thr Leu Gln Gly Ile His Leu Lys Asn Ile Gln Ser Val
45 50 55

aat gta agg tcc ccc gga ccc cac tgc gcc caa acc gaa gtc ata gcc 302
Asn Val Arg Ser Pro Gly Pro His Cys Ala Gln Thr Glu Val Ile Ala
60 65 70 75

aca ctc aag aat ggg aag aaa gct tgt ctc aac ccc gca tcc ccc atg 350
Thr Leu Lys Asn Gly Lys Lys Ala Cys Leu Asn Pro Ala Ser Pro Met
80 85 90

gtt cag aaa atc atc gaa aag ata ctg aac aag ggg agc acc aac 395
Val Gln Lys Ile Ile Glu Lys Ile Leu Asn Lys Gly Ser Thr Asn
95 100 105

tgacaggaga gaagtaagaa gcttatcagc gtatcattga cacttcctgc agggtggtcc 455

ctgcccttac cagagctgaa aatgaaaaag agaacagcag ctttctaggg acagctggaa 515

agggacttaa tgtgtttgac tatttcttac gagggttcta cttatttatg tatttatttt 575

tgaaagcttg tattttaata ttttacatgc tgttatttaa agatgtgagt gtgtttcatc 635

aaacatagct cagtcctgat tatttaattg gaatatgatg ggttttaaat gtgtcattaa 695

actaatattt agtgggagac cataatgtgt cagccacctt gataaatgac agggtgggga 755

actggagggt ngggggattg aaatgcaagc aattagtgga tcactgttag ggtaagggaa 815

tgtatgtaca catctatttt ttatactttt ttttttaaaa aagaatgtca gttgttattt 875

attcaaatta tctcacatta tgtgttcaac atttttatgc tgaagtttcc cttagacatt 935

ttatgtcttg cttgtagggc ataatgcctt gtttaatgtc cattctgcag cgtttctctt 995

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tcccttggaa aagagaattt atcattactg ttacatttgt acaaatgaca tgataataaa 1055

agttttatg                                                          1064


<210> 9
<211> 1469
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> (102)..(1001)

<400> 9
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agccttctca gccaaacgcc gaccaaggaa aactcactac c atg aga att gca gtg 116
                                              Met Arg Ile Ala Val
                                                1               5

att tgc ttt tgc ctc cta ggc atc acc tgt gcc ata cca gtt aaa cag   164
Ile Cys Phe Cys Leu Leu Gly Ile Thr Cys Ala Ile Pro Val Lys Gln
                10                  15                  20

gct gat tct gga agt tct gag gaa aag cag ctt tac aac aaa tac cca   212
Ala Asp Ser Gly Ser Ser Glu Glu Lys Gln Leu Tyr Asn Lys Tyr Pro
            25                  30                  35

gat gct gtg gcc aca tgg cta aac cct gac cca tct cag aag cag aat   260
Asp Ala Val Ala Thr Trp Leu Asn Pro Asp Pro Ser Gln Lys Gln Asn
        40                  45                  50

ctc cta gcc cca cag acc ctt cca agt aag tcc aac gaa agc cat gac   308
Leu Leu Ala Pro Gln Thr Leu Pro Ser Lys Ser Asn Glu Ser His Asp
    55                  60                  65

cac atg gat gat atg gat gat gaa gat gat gat gac cat gtg gac agc   356
His Met Asp Asp Met Asp Asp Glu Asp Asp Asp Asp His Val Asp Ser
70                  75                  80                  85

cag gac tcc att gac tcg aac gac tct gat gat gta gat gac act gat   404
Gln Asp Ser Ile Asp Ser Asn Asp Ser Asp Asp Val Asp Asp Thr Asp
                90                  95                  100

gat tct cac cag tct gat gag tct cac cat tct gat gaa tct gat gaa   452
Asp Ser His Gln Ser Asp Glu Ser His His Ser Asp Glu Ser Asp Glu
            105                 110                 115

ctg gtc act gat ttt ccc acg gac ctg cca gca acc gaa gtt ttc act   500
Leu Val Thr Asp Phe Pro Thr Asp Leu Pro Ala Thr Glu Val Phe Thr
        120                 125                 130

cca gtt gtc ccc aca gta gac aca tat gat ggc cga ggt gat agt gtg   548
Pro Val Val Pro Thr Val Asp Thr Tyr Asp Gly Arg Gly Asp Ser Val
    135                 140                 145
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gtt tat gga ctg agg tca aaa tct aag aag ttt cgc aga cct gac atc   596
Val Tyr Gly Leu Arg Ser Lys Ser Lys Lys Phe Arg Arg Pro Asp Ile
150                 155                 160                 165

cag tac cct gat gct aca gac gag gac atc acc tca cac atg gaa agc   644
Gln Tyr Pro Asp Ala Thr Asp Glu Asp Ile Thr Ser His Met Glu Ser
                170                 175                 180

gag gag ttg aat ggt gca tac aag gcc atc ccc gtt gcc cag gac ctg   692
Glu Glu Leu Asn Gly Ala Tyr Lys Ala Ile Pro Val Ala Gln Asp Leu
            185                 190                 195

aac gcg cct tct gat tgg gac agc cgt ggg aag gac agt tat gaa acg   740
Asn Ala Pro Ser Asp Trp Asp Ser Arg Gly Lys Asp Ser Tyr Glu Thr
        200                 205                 210

agt cag ctg gat gac cag agt gct gaa acc cac agc cac aag cag tcc   788
Ser Gln Leu Asp Asp Gln Ser Ala Glu Thr His Ser His Lys Gln Ser
    215                 220                 225

aga tta tat aag cgg aaa gcc aat gat gag agc aat gag cat tcc gat   836
Arg Leu Tyr Lys Arg Lys Ala Asn Asp Glu Ser Asn Glu His Ser Asp
230                 235                 240                 245

gtg att gat agt cag gaa ctt tcc aaa gtc agc cgt gaa ttc cac agc   884
Val Ile Asp Ser Gln Glu Leu Ser Lys Val Ser Arg Glu Phe His Ser
                250                 255                 260

cat gaa ttt cac agc cat gaa gat atg ctg gtt gta gac ccc aaa agt   932
His Glu Phe His Ser His Glu Asp Met Leu Val Val Asp Pro Lys Ser
            265                 270                 275

aag gaa gaa gat aaa cac ctg aaa ttt cgt att tct cat gaa tta gat   980
Lys Glu Glu Asp Lys His Leu Lys Phe Arg Ile Ser His Glu Leu Asp
        280                 285                 290

agt gca tct tct gag gtc aat taaaaggaga aaaaatacaa tttctcactt      1031
Ser Ala Ser Ser Glu Val Asn
    295                 300

tgcatttagt caaaagaaaa aatgctttat agcaaaatga aagagaacat gaaatgcttc 1091

tttctcagtt tattggttga atgtgtatct atttgagtct ggaaataact aatgtgtttg 1151

ataattagtt tagtttgtgg cttcatggaa actccctgta aactaaaagc ttcagggtta 1211

tgtctatgtt cattctatag aagaaatgca aactatcact gtattttaat atttgttatt 1271

ctctcatgaa tagaaattta tgtagaagca aacaaaatac ttttacccac ttaaaaagag 1331

aatataacat tttatgtcac tataatcttt tgtttttaa gttagtgtat attttgttgt 1391

gattatcttt ttgtggtgtg aataaatctt ttatcttgaa tgtaataaga aaaaaaaaaa 1451

aaaaacaaaa aaaaaaaa                                              1469
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<210> 10
<211> 1256
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> (145)..(1029)

<400> 10
gcagtagcag cgagcagcag agtccgcacg ctccggcgag gggcagaaga gcgcgaggga 60

gcgcggggca gcagaagcga gagccgagcg cggacccagc caggacccac agccctcccc 120

agctgcccag gaagagcccc agcc atg gaa cac cag ctc ctg tgc tgc gaa 171
Met Glu His Gln Leu Leu Cys Cys Glu
1 5

gtg gaa acc atc cgc cgc gcg tac ccc gat gcc aac ctc ctc aac gac 219
Val Glu Thr Ile Arg Arg Ala Tyr Pro Asp Ala Asn Leu Leu Asn Asp
10 15 20 25

cgg gtg ctg cgg gcc atg ctg aag gcg gag gag acc tgc gcg ccc tcg 267
Arg Val Leu Arg Ala Met Leu Lys Ala Glu Glu Thr Cys Ala Pro Ser
30 35 40

gtg tcc tac ttc aaa tgt gtg cag aag gag gtc ctg ccg tcc atg cgg 315
Val Ser Tyr Phe Lys Cys Val Gln Lys Glu Val Leu Pro Ser Met Arg
45 50 55

aag atc gtc gcc acc tgg atg ctg gag gtc tgc gag gaa cag aag tgc 363
Lys Ile Val Ala Thr Trp Met Leu Glu Val Cys Glu Glu Gln Lys Cys
60 65 70

gag gag gag gtc ttc ccg ctg gcc atg aac tac ctg gac cgc ttc ctg 411
Glu Glu Glu Val Phe Pro Leu Ala Met Asn Tyr Leu Asp Arg Phe Leu
75 80 85

tcg ctg gag ccc gtg aaa aag agc cgc ctg cag ctg ctg ggg gcc act 459
Ser Leu Glu Pro Val Lys Lys Ser Arg Leu Gln Leu Leu Gly Ala Thr
90 95 100 105

tgc atg ttc gtg gcc tct aag atg aag gag acc atc ccc ctg acg gcc 507
Cys Met Phe Val Ala Ser Lys Met Lys Glu Thr Ile Pro Leu Thr Ala
110 115 120

gag aag ctg tgc atc tac acc gac ggc tcc atc cgg ccc gag gag ctg 555
Glu Lys Leu Cys Ile Tyr Thr Asp Gly Ser Ile Arg Pro Glu Glu Leu
125 130 135

ctg caa atg gag ctg ctc ctg gtg aac aag ctc aag tgg aac ctg gcc 603
Leu Gln Met Glu Leu Leu Leu Val Asn Lys Leu Lys Trp Asn Leu Ala
140 145 150

gca atg acc ccg cac gat ttc att gaa cac ttc ctc tcc aaa atg cca 651
Ala Met Thr Pro His Asp Phe Ile Glu His Phe Leu Ser Lys Met Pro
155 160 165

```
gag gcg gag gag aac aaa cag atc atc cgc aaa cac gcg cag acc ttc   699
Glu Ala Glu Glu Asn Lys Gln Ile Ile Arg Lys His Ala Gln Thr Phe
170                 175                 180                 185

gtt gcc tct tgt gcc aca gat gtg aag ttc att tcc aat ccg ccc tcc   747
Val Ala Ser Cys Ala Thr Asp Val Lys Phe Ile Ser Asn Pro Pro Ser
                190                 195                 200

atg gtg gca gcg ggg agc gtg gtg gcc gca gtg caa ggc ctg aac ctg   795
Met Val Ala Ala Gly Ser Val Val Ala Ala Val Gln Gly Leu Asn Leu
            205                 210                 215

agg agc ccc aac aac ttc ctg tcc tac tac cgc ctc aca cgc ttc ctc   843
Arg Ser Pro Asn Asn Phe Leu Ser Tyr Tyr Arg Leu Thr Arg Phe Leu
        220                 225                 230

tcc aga gtg atc aag tgt gac cca gac tgc ctc cgg gcc tgc cag gag   891
Ser Arg Val Ile Lys Cys Asp Pro Asp Cys Leu Arg Ala Cys Gln Glu
    235                 240                 245

cag atc gaa gcc ctg ctg gag tca agc ctg cgc cag gcc cag cag aac   939
Gln Ile Glu Ala Leu Leu Glu Ser Ser Leu Arg Gln Ala Gln Gln Asn
250                 255                 260                 265

atg gac ccc aag gcc gcc gag gag gag gaa gag gag gag gag gag gtg   987
Met Asp Pro Lys Ala Ala Glu Glu Glu Glu Glu Glu Glu Glu Glu Val
                270                 275                 280

gac ctg gct tgc aca ccc acc gac gtg cgg gac gtg gac atc           1029
Asp Leu Ala Cys Thr Pro Thr Asp Val Arg Asp Val Asp Ile
            285                 290                 295

tgaggggccc aggcaggcgg gcgccaccgc cacccgcagc gagggcggag ccggccccag 1089

gtgctccaca tgacagtccc tcctctccgg agcattttga taccagaagg gaaagcttca 1149

ttctccttgt tgttggttgt tttttccttt gctctttccc ccttccatct ctgacttaag 1209

caaaagaaaa agattaccca aaaactgtct ttaaaagaga gagagag               1256
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<210> 11
<211> 2121
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> (559)..(1875)

<400> 11
ctgctcgcgg ccgccaccgc cgggccccgg ccgtccctgg ctcccctcct gcctcgagaa 60

gggcagggct tctcagaggc ttggcgggaa aaaagaacgg agggagggat cgcgctgagt 120

ataaaagccg gttttcgggg ctttatctaa ctcgctgtag taattccagc gagaggcaga 180

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gggagcgagc gggcggccgg ctagggtgga agagccgggc gagcagagct gcgctgcggg 240

cgtcctggga agggagatcc ggagcgaata gggggcttcg cctctggccc agccctcccg 300

cttgatcccc caggccagcg gtccgcaacc cttgccgcat ccacgaaact ttgcccatag 360

cagcgggcgg gcactttgca ctggaactta caacacccga gcaaggacgc gactctcccg 420

acgcggggag gctattctgc ccatttgggg acacttcccc gccgctgcca ggacccgctt 480

ctctgaaagg ctctccttgc agctgcttag acgctggatt tttttcgggt agtggaaaac 540

cagcagcctc ccgcgacg atg ccc ctc aac gtt agc ttc acc aac agg aac   591
                    Met Pro Leu Asn Val Ser Phe Thr Asn Arg Asn
                      1               5                  10

tat gac ctc gac tac gac tcg gtg cag ccg tat ttc tac tgc gac gag   639
Tyr Asp Leu Asp Tyr Asp Ser Val Gln Pro Tyr Phe Tyr Cys Asp Glu
             15                  20                  25

gag gag aac ttc tac cag cag cag cag cag agc gag ctg cag ccc ccg   687
Glu Glu Asn Phe Tyr Gln Gln Gln Gln Gln Ser Glu Leu Gln Pro Pro
         30                  35                  40

gcg ccc agc gag gat atc tgg aag aaa ttc gag ctg ctg ccc acc ccg   735
Ala Pro Ser Glu Asp Ile Trp Lys Lys Phe Glu Leu Leu Pro Thr Pro
     45                  50                  55

ccc ctg tcc cct agc cgc cgc tcc ggg ctc tgc tcg ccc tcc tac gtt   783
Pro Leu Ser Pro Ser Arg Arg Ser Gly Leu Cys Ser Pro Ser Tyr Val
 60                  65                  70                  75

gcg gtc aca ccc ttc tcc ctt cgg gga gac aac gac ggc ggt ggc ggg   831
Ala Val Thr Pro Phe Ser Leu Arg Gly Asp Asn Asp Gly Gly Gly Gly
                 80                  85                  90

agc ttc tcc acg gcc gac cag ctg gag atg gtg acc gag ctg ctg gga   879
Ser Phe Ser Thr Ala Asp Gln Leu Glu Met Val Thr Glu Leu Leu Gly
             95                  100                 105

gga gac atg gtg aac cag agt ttc atc tgc gac ccg gac gac gag acc   927
Gly Asp Met Val Asn Gln Ser Phe Ile Cys Asp Pro Asp Asp Glu Thr
        110                 115                 120

ttc atc aaa aac atc atc atc cag gac tgt atg tgg agc ggc ttc tcg   975
Phe Ile Lys Asn Ile Ile Ile Gln Asp Cys Met Trp Ser Gly Phe Ser
    125                 130                 135

gcc gcc gcc aag ctc gtc tca gag aag ctg gcc tcc tac cag gct gcg   1023
Ala Ala Ala Lys Leu Val Ser Glu Lys Leu Ala Ser Tyr Gln Ala Ala
140                 145                 150                 155

cgc aaa gac agc ggc agc ccg aac ccc gcc cgc ggc cac agc gtc tgc   1071
Arg Lys Asp Ser Gly Ser Pro Asn Pro Ala Arg Gly His Ser Val Cys
                160                 165                 170
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tcc acc tcc agc ttg tac ctg cag gat ctg agc gcc gcc gcc tca gag   1119
Ser Thr Ser Ser Leu Tyr Leu Gln Asp Leu Ser Ala Ala Ala Ser Glu
            175                 180                 185

tgc atc gac ccc tcg gtg gtc ttc ccc tac cct ctc aac gac agc agc   1167
Cys Ile Asp Pro Ser Val Val Phe Pro Tyr Pro Leu Asn Asp Ser Ser
        190                 195                 200

tcg ccc aag tcc tgc gcc tcg caa gac tcc agc gcc ttc tct ccg tcc   1215
Ser Pro Lys Ser Cys Ala Ser Gln Asp Ser Ser Ala Phe Ser Pro Ser
    205                 210                 215

tcg gat tct ctg ctc tcc tcg acg gag tcc tcc ccg cag ggc agc ccc   1263
Ser Asp Ser Leu Leu Ser Ser Thr Glu Ser Ser Pro Gln Gly Ser Pro
220                 225                 230                 235

gag ccc ctg gtg ctc cat gag gag aca ccg ccc acc acc agc agc gac   1311
Glu Pro Leu Val Leu His Glu Glu Thr Pro Pro Thr Thr Ser Ser Asp
                240                 245                 250

tct gag gag gaa caa gaa gat gag gaa gaa atc gat gtt gtt tct gtg   1359
Ser Glu Glu Glu Gln Glu Asp Glu Glu Glu Ile Asp Val Val Ser Val
            255                 260                 265

gaa aag agg cag gct cct ggc aaa agg tca gag tct gga tca cct tct   1407
Glu Lys Arg Gln Ala Pro Gly Lys Arg Ser Glu Ser Gly Ser Pro Ser
        270                 275                 280

gct gga ggc cac agc aaa cct cct cac agc cca ctg gtc ctc aag agg   1455
Ala Gly Gly His Ser Lys Pro Pro His Ser Pro Leu Val Leu Lys Arg
    285                 290                 295

tgc cac gtc tcc aca cat cag cac aac tac gca gcg cct ccc tcc act   1503
Cys His Val Ser Thr His Gln His Asn Tyr Ala Ala Pro Pro Ser Thr
300                 305                 310                 315

cgg aag gac tat cct gct gcc aag agg gtc aag ttg gac agt gtc aga   1551
Arg Lys Asp Tyr Pro Ala Ala Lys Arg Val Lys Leu Asp Ser Val Arg
                320                 325                 330

gtc ctg aga cag atc agc aac aac cga aaa tgc acc agc ccc agg tcc   1599
Val Leu Arg Gln Ile Ser Asn Asn Arg Lys Cys Thr Ser Pro Arg Ser
            335                 340                 345

tcg gac acc gag gag aat gtc aag agg cga aca cac aac gtc ttg gag   1647
Ser Asp Thr Glu Glu Asn Val Lys Arg Arg Thr His Asn Val Leu Glu
        350                 355                 360

cgc cag agg agg aac gag cta aaa cgg agc ttt ttt gcc ctg cgt gac   1695
Arg Gln Arg Arg Asn Glu Leu Lys Arg Ser Phe Phe Ala Leu Arg Asp
    365                 370                 375

cag atc ccg gag ttg gaa aac aat gaa aag gcc ccc aag gta gtt atc   1743
Gln Ile Pro Glu Leu Glu Asn Asn Glu Lys Ala Pro Lys Val Val Ile
380                 385                 390                 395
```

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ctt aaa aaa gcc aca gca tac atc ctg tcc gtc caa gca gag gag caa   1791
Leu Lys Lys Ala Thr Ala Tyr Ile Leu Ser Val Gln Ala Glu Glu Gln
                400                 405                 410

aag ctc att tct gaa gag gac ttg ttg cgg aaa cga cga gaa cag ttg   1839
Lys Leu Ile Ser Glu Glu Asp Leu Leu Arg Lys Arg Arg Glu Gln Leu
            415                 420                 425

aaa cac aaa ctt gaa cag cta cgg aac tct tgt gcg taaggaaaag        1885
Lys His Lys Leu Glu Gln Leu Arg Asn Ser Cys Ala
        430                 435

taaggaaaac gattccttct aacagaaatg tcctgagcaa tcacctatga acttgtttca 1945

aatgcatgat caaatgcaac ctcacaacct tggctgagtc ttgagactga aagatttagc 2005

cataatgtaa actgcctcaa attggacttt gggcataaaa gaacttttt atgcttacca 2065

tctttttttt ttctttaaca gatttgtatt taagaattgt ttttaaaaaa ttttaa     2121
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<210> 12
<211> 2098
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> (79)..(570)

<400> 12

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gcactcagag gaggcgcc atg tca gaa ccg gct ggg gat gtc cgt cag aac   111
                    Met Ser Glu Pro Ala Gly Asp Val Arg Gln Asn
                      1               5                  10

cca tgc ggc agc aag gcc tgc cgc cgc ctc ttc ggc cca gtg gac agc   159
Pro Cys Gly Ser Lys Ala Cys Arg Arg Leu Phe Gly Pro Val Asp Ser
             15                  20                  25

gag cag ctg agc cgc gac tgt gat gcg cta atg gcg ggc tgc atc cag   207
Glu Gln Leu Ser Arg Asp Cys Asp Ala Leu Met Ala Gly Cys Ile Gln
         30                  35                  40

gag gcc cgt gag cga tgg aac ttc gac ttt gtc acc gag aca cca ctg   255
Glu Ala Arg Glu Arg Trp Asn Phe Asp Phe Val Thr Glu Thr Pro Leu
     45                  50                  55

gag ggt gac ttc gcc tgg gag cgt gtg cgg ggc ctt ggc ctg ccc aag   303
Glu Gly Asp Phe Ala Trp Glu Arg Val Arg Gly Leu Gly Leu Pro Lys
 60                  65                  70                  75

ctc tac ctt ccc acg ggg ccc cgg cga ggc cgg gat gag ttg gga gga   351
Leu Tyr Leu Pro Thr Gly Pro Arg Arg Gly Arg Asp Glu Leu Gly Gly
                 80                  85                  90
```

```
ggc agg cgg cct ggc acc tca cct gct ctg ctg cag ggg aca gca gag   399
Gly Arg Arg Pro Gly Thr Ser Pro Ala Leu Leu Gln Gly Thr Ala Glu
             95                  100                 105

gaa gac cat gtg gac ctg tca ctg tct tgt acc ctt gtg cct cgc tca   447
Glu Asp His Val Asp Leu Ser Leu Ser Cys Thr Leu Val Pro Arg Ser
        110                 115                 120

ggg gag cag gct gaa ggg tcc cca ggt gga cct gga gac tct cag ggt   495
Gly Glu Gln Ala Glu Gly Ser Pro Gly Gly Pro Gly Asp Ser Gln Gly
    125                 130                 135

cga aaa cgg cgg cag acc agc atg aca gat ttc tac cac tcc aaa cgc   543
Arg Lys Arg Arg Gln Thr Ser Met Thr Asp Phe Tyr His Ser Lys Arg
140                 145                 150                 155

cgg ctg atc ttc tcc aag agg aag ccc taatccgccc acaggaagcc         590
Arg Leu Ile Phe Ser Lys Arg Lys Pro
                160

tgcagtcctg gaagcgcgag ggcctcaaag gcccgctcta catcttctgc cttagtctca 650

gtttgtgtgt cttaattatt atttgtgttt taatttaaac acctcctcat gtacataccc 710

tggccgcccc ctgcccccca gcctctggca ttagaattat ttaaacaaaa actaggcggt 770

tgaatgagag gttcctaaga gtgctgggca tttttatttt atgaaatact atttaaagcc 830

tcctcatccc gtgttctcct tttcctctct cccggaggtt gggtgggccg gcttcatgcc 890

agctacttcc tcctccccac ttgtccgctg ggtggtaccc tctggagggg tgtggctcct 950

tcccatcgct gtcacaggcg gttatgaaat tcacccccct tcctggacac tcagacctga 1010

attctttttc atttgagaag taaacagatg gcactttgaa ggggcctcac cgagtggggg 1070

catcatcaaa aactttggag tcccctcacc tcctctaagg ttgggcaggg tgaccctgaa 1130

gtgagcacag cctagggctg agctggggac ctggtaccct cctggctctt gataccccca 1190

tctgtcttgt gaaggcaggg ggaaggtggg gtcctggagc agaccacccc gcctgccctc 1250

atggcccctc tgacctgcac tggggagccc gtctcagtgt tgagcctttt ccctctttgg 1310

ctcccctgta ccttttgagg agccccagct acccttcttc tccagctggg ctctgcaatt 1370

cccctctgct gctgtccctc ccccttgtcc tttcccttca gtaccctctc agctccaggt 1430

ggctctgagg tgcctgtccc acccccaccc ccagctcaat ggactggaag gggaagggac 1490

acacaagaag aagggcaccc tagttctacc tcaggcagct caagcagcga ccgccccctc 1550

ctctagctgt gggggtgagg gtcccatgtg gtggcacagg ccccccttgag tggggttatc 1610

tctgtgttag gggtatatga tgggggagta gatctttcta ggagggagac actggcccct 1670

caaatcgtcc agcgaccttc ctcatccacc ccatccctcc ccagttcatt gcactttgat 1730
```

tagcagcgga acaaggagtc agacatttta agatggtggc agtagaggct atggacaggg 1790

catgccacgt gggctcatat ggggctggga gtagttgtct ttcctggcac taacgttgag 1850

cccctggagg cactgaagtg cttagtgtac ttggagtatt ggggtctgac cccaaacacc 1910

ttccagctcc tgtaacatac tggcctggac tgttttctct cggctcccca tgtgtcctgg 1970

ttcccgtttc tccacctaga ctgtaaacct ctcgagggca gggaccacac cctgtactgt 2030

tctgtgtctt tcacagctcc tcccacaatg ctgatataca gcaggtgctc aataaacgat 2090

tcttagtg 2098

<210> 13
<211> 827
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> (256)..(570)

<400> 13
ggcacgaggc aaagggcggc gcagcggctg ccgagctcgg ccctggaggc ggcgagaaca 60

tggtgcgcag gttcttggtg accctccgga ttcggcgcgc gtgcggcccg ccgcgagtga 120

gggttttcgt ggttcacatc tcgtggttca cgggggagtg ggcagcgcca ggggcgcccg 180

ccgctgtggc cctcgtgctg atgctactga ggagccagcg tctagggcag cagccgcttc 240

ctagaagacc aggtc atg atg atg ggc agc gcc cga gtg gcg gag ctg ctg 291
Met Met Met Gly Ser Ala Arg Val Ala Glu Leu Leu
1 5 10

ctg ctc cac ggc gcg gag ccc aac tgc gcc gac ccc gcc act ctc acc 339
Leu Leu His Gly Ala Glu Pro Asn Cys Ala Asp Pro Ala Thr Leu Thr
15 20 25

cga ccc gtg cac gac gct gcc cgg gag ggc ttc ctg gac acg ctg gtg 387
Arg Pro Val His Asp Ala Ala Arg Glu Gly Phe Leu Asp Thr Leu Val
30 35 40

gtg ctg cac cgg gcc ggg gcg cgg ctg gac gtg cgc gat gcc tgg ggc 435
Val Leu His Arg Ala Gly Ala Arg Leu Asp Val Arg Asp Ala Trp Gly
45 50 55 60

cgt ctg ccc gtg gac ctg gct gag gag ctg ggc cat cgc gat gtc gca 483
Arg Leu Pro Val Asp Leu Ala Glu Glu Leu Gly His Arg Asp Val Ala
65 70 75

cgg tac ctg cgc gcg gct gcg ggg ggc acc aga ggc agt aac cat gcc 531
Arg Tyr Leu Arg Ala Ala Ala Gly Gly Thr Arg Gly Ser Asn His Ala
80 85 90

```
cgc ata gat gcc gcg gaa ggt ccc tca gac atc ccc gat tgaaagaacc    580
Arg Ile Asp Ala Ala Glu Gly Pro Ser Asp Ile Pro Asp
         95                  100                 105

agagaggctc tgagaaacct ccggaaactt agatcatcag tcaccgaagg tcctacaggg 640

ccacaactgc ccccgccaca acccaccccg ctttcgtagt tttcatttag aaaatagagc 700

ttttaaaaat gtcctgcctt ttaacgtaga tatatgcctt cccccactac cgtaaatgtc 760

catttatatc attttttata tattcttata aaaatgtaaa aaagaaaaaa aaaaaaaaaa 820

aaaaaaa                                                          827



<210> 14
<211> 1275
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> (163)..(681)

<400> 14
cctccctacg ggcgcctccg gcagcccttc ccgcgtgcgc agggctcaga gccgttccga 60

gatcttggag gtccgggtgg gagtgggggt ggggtggggg tgggggtgaa ggtgggggggc 120

gggcgcgctc agggaaggcg ggtgcgcgcc tgcggggcgg ag atg ggc agg ggg    174
                                              Met Gly Arg Gly
                                                1

cgg tgc gtg ggt ccc agt ctg cag tta agg ggg cag gag tgg cgc tgc   222
Arg Cys Val Gly Pro Ser Leu Gln Leu Arg Gly Gln Glu Trp Arg Cys
  5                  10                  15                  20

tca cct ctg gtg cca aag ggc ggc gca gcg gct gcc gag ctc ggc cct   270
Ser Pro Leu Val Pro Lys Gly Gly Ala Ala Ala Ala Glu Leu Gly Pro
                 25                  30                  35

gga ggc ggc gag aac atg gtg cgc agg ttc ttg gtg acc ctc cgg att   318
Gly Gly Gly Glu Asn Met Val Arg Arg Phe Leu Val Thr Leu Arg Ile
             40                  45                  50

cgg cgc gcg tgc ggc ccg ccg cga gtg agg gtt ttc gtg gtt cac atc   366
Arg Arg Ala Cys Gly Pro Pro Arg Val Arg Val Phe Val Val His Ile
         55                  60                  65

ccg cgg ctc acg ggg gag tgg gca gcg cca ggg gcg ccc gcc gct gtg   414
Pro Arg Leu Thr Gly Glu Trp Ala Ala Pro Gly Ala Pro Ala Ala Val
     70                  75                  80

gcc ctc gtg ctg atg cta ctg agg agc cag cgt cta ggg cag cag ccg   462
Ala Leu Val Leu Met Leu Leu Arg Ser Gln Arg Leu Gly Gln Gln Pro
 85                  90                  95                  100
```

```
ctt cct aga aga cca ggt cat gat gat ggg cag cgc ccg agt ggc gga   510
Leu Pro Arg Arg Pro Gly His Asp Asp Gly Gln Arg Pro Ser Gly Gly
                105                 110                 115

gct gct gct gct cca cgg cgc gga gcc caa ctg cgc cga ccc cgc cac   558
Ala Ala Ala Ala Pro Arg Arg Gly Ala Gln Leu Arg Arg Pro Arg His
            120                 125                 130

tct cac ccg acc cgt gca cga cgc tgc ccg gga ggg ctt cct gga cac   606
Ser His Pro Thr Arg Ala Arg Arg Cys Pro Gly Gly Leu Pro Gly His
        135                 140                 145

gct ggt ggt gct gca ccg ggc cgg ggc gcg gct gga cgt gcg cga tgc   654
Ala Gly Gly Ala Ala Pro Gly Arg Gly Ala Ala Gly Arg Ala Arg Cys
    150                 155                 160

ctg ggg ccg tct gcc cgt gga cct ggc tgaggagctg ggccatcgcg         701
Leu Gly Pro Ser Ala Arg Gly Pro Gly
165                 170

atgtcgcacg gtacctgcgc gcggctgcgg ggggcaccag aggcagtaac catgcccgca 761

tagatgccgc ggaaggtccc tcagacatcc ccgattgaaa gaaccagaga ggctctgaga 821

aacctcggga aacttagatc atcagtcacc gaaggtccta cagggccaca actgcccccg 881

ccacaaccca ccccgctttc gtagttttca tttagaaaat agagctttta aaaatgtcct 941

gccttttaac gtagatatat gccttccccc actaccgtaa atgtccattt atatcatttt 1001

ttatatattc ttataaaaat gtaaaaaaga aaaacaccgc ttctgccttt tcactgtgtt 1061

ggagttttct ggagtgagca ctcacgccct aagcgcacat tcatgtgggc atttcttgcg 1121

agcctcgcag cctccggaag ctgtcgactt catgacaagc attttgtgaa ctagggaagc 1181

tcaggggggt tactggcttc tcttgagtca cactgctagc aaatggcaga accaaagctc 1241

aaataaaaat aaaataattt tcattcattc actc                           1275
```

<210> 15
<211> 1850
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> (213)..(1616)

<400> 15

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ggcccaggct gaagctcagg gccctgtctg ctctgtggac tcaacagttt gtggcaagac 60

aagctcagaa ctgagaagct gtcaccacag ttctggaggc tgggaagttc aagatcaaag 120

tgccagcaga ttcagtgtca tgtgaggacg tgcttcctgc ttcatagata agagcttgga 180
```

```
gctcggcgca caaccagcac catctggtcg cg atg gtg gac acg gaa agc cca   233
                                    Met Val Asp Thr Glu Ser Pro
                                      1               5

ctc tgc ccc ctc tcc cca ctc gag gcc ggc gat cta gag agc ccg tta   281
Leu Cys Pro Leu Ser Pro Leu Glu Ala Gly Asp Leu Glu Ser Pro Leu
         10                  15                  20

tct gaa gag ttc ctg caa gaa atg gga aac atc caa gag att tcg caa   329
Ser Glu Glu Phe Leu Gln Glu Met Gly Asn Ile Gln Glu Ile Ser Gln
     25                  30                  35

tcc atc ggc gag gat agt tct gga agc ttt ggc ttt acg gaa tac cag   377
Ser Ile Gly Glu Asp Ser Ser Gly Ser Phe Gly Phe Thr Glu Tyr Gln
 40                  45                  50                  55

tat tta gga agc tgt cct ggc tca gat ggc tcg gtc atc acg gac acg   425
Tyr Leu Gly Ser Cys Pro Gly Ser Asp Gly Ser Val Ile Thr Asp Thr
                 60                  65                  70

ctt tca cca gct tcg agc ccc tcc tcg gtg act tat cct gtg gtc ccc   473
Leu Ser Pro Ala Ser Ser Pro Ser Ser Val Thr Tyr Pro Val Val Pro
             75                  80                  85

ggc agc gtg gac gag tct ccc agt gga gca ttg aac atc gaa tgt aga   521
Gly Ser Val Asp Glu Ser Pro Ser Gly Ala Leu Asn Ile Glu Cys Arg
         90                  95                  100

atc tgc ggg gac aag gcc tca ggc tat cat tac gga gtc cac gcg tgt   569
Ile Cys Gly Asp Lys Ala Ser Gly Tyr His Tyr Gly Val His Ala Cys
    105                 110                 115

gaa ggc tgc aag ggc ttc ttt cgg cga acg att cga ctc aag ctg gtg   617
Glu Gly Cys Lys Gly Phe Phe Arg Arg Thr Ile Arg Leu Lys Leu Val
120                 125                 130                 135

tat gac aag tgc gac cgc agc tgc aag atc cag aaa aag aac aga aac   665
Tyr Asp Lys Cys Asp Arg Ser Cys Lys Ile Gln Lys Lys Asn Arg Asn
                140                 145                 150

aaa tgc cag tat tgt cga ttt cac aag tgc ctt tct gtc ggg atg tca   713
Lys Cys Gln Tyr Cys Arg Phe His Lys Cys Leu Ser Val Gly Met Ser
            155                 160                 165

cac aac gcg att cgt ttt gga cga atg cca aga tct gag aaa gca aaa   761
His Asn Ala Ile Arg Phe Gly Arg Met Pro Arg Ser Glu Lys Ala Lys
        170                 175                 180

ctg aaa gca gaa att ctt acc tgt gaa cat gac ata gaa gat tct gaa   809
Leu Lys Ala Glu Ile Leu Thr Cys Glu His Asp Ile Glu Asp Ser Glu
    185                 190                 195

act gca gat ctc aaa tct ctg gcc aag aga atc tac gag gcc tac ttg   857
Thr Ala Asp Leu Lys Ser Leu Ala Lys Arg Ile Tyr Glu Ala Tyr Leu
200                 205                 210                 215
```

```
aag aac ttc aac atg aac aag gtc aaa gcc cgg gtc atc ctc tca gga   905
Lys Asn Phe Asn Met Asn Lys Val Lys Ala Arg Val Ile Leu Ser Gly
                220                 225                 230

aag gcc agt aac aat cca cct ttt gtc ata cat gat atg gag aca ctg   953
Lys Ala Ser Asn Asn Pro Pro Phe Val Ile His Asp Met Glu Thr Leu
            235                 240                 245

tgt atg gct gag aag acg ctg gtg gcc aag ctg gtg gcc aat ggc atc   1001
Cys Met Ala Glu Lys Thr Leu Val Ala Lys Leu Val Ala Asn Gly Ile
        250                 255                 260

cag aac aag gag gcg gag gtc cgc atc ttt cac tgc tgc cag tgc acg   1049
Gln Asn Lys Glu Ala Glu Val Arg Ile Phe His Cys Cys Gln Cys Thr
    265                 270                 275

tca gtg gag acc gtc acg gag ctc acg gaa ttc gcc aag gcc atc cca   1097
Ser Val Glu Thr Val Thr Glu Leu Thr Glu Phe Ala Lys Ala Ile Pro
280                 285                 290                 295

ggc ttc gca aac ttg gac ctg aac gat caa gtg aca ttg cta aaa tac   1145
Gly Phe Ala Asn Leu Asp Leu Asn Asp Gln Val Thr Leu Leu Lys Tyr
                300                 305                 310

gga gtt tat gag gcc ata ttc gcc atg ctg tct tct gtg atg aac aaa   1193
Gly Val Tyr Glu Ala Ile Phe Ala Met Leu Ser Ser Val Met Asn Lys
            315                 320                 325

gac ggg atg ctg gta gcg tat gga aat ggg ttt ata act cgt gaa ttc   1241
Asp Gly Met Leu Val Ala Tyr Gly Asn Gly Phe Ile Thr Arg Glu Phe
        330                 335                 340

cta aaa agc cta agg aaa ccg ttc tgt gat atc atg gaa ccc aag ttt   1289
Leu Lys Ser Leu Arg Lys Pro Phe Cys Asp Ile Met Glu Pro Lys Phe
    345                 350                 355

gat ttt gcc atg aag ttc aat gca ctg gaa ctg gat gac agt gat atc   1337
Asp Phe Ala Met Lys Phe Asn Ala Leu Glu Leu Asp Asp Ser Asp Ile
360                 365                 370                 375

tcc ctt ttt gtg gct gct atc att tgc tgt gga gat cgt cct ggc ctt   1385
Ser Leu Phe Val Ala Ala Ile Ile Cys Cys Gly Asp Arg Pro Gly Leu
                380                 385                 390

cta aac gta gga cac att gaa aaa atg cag gag ggt att gta cat gtg   1433
Leu Asn Val Gly His Ile Glu Lys Met Gln Glu Gly Ile Val His Val
            395                 400                 405

ctc aga ctc cac ctg cag agc aac cac ccg gac gat atc ttt ctc ttc   1481
Leu Arg Leu His Leu Gln Ser Asn His Pro Asp Asp Ile Phe Leu Phe
        410                 415                 420

cca aaa ctt ctt caa aaa atg gca gac ctc cgg cag ctg gtg acg gag   1529
Pro Lys Leu Leu Gln Lys Met Ala Asp Leu Arg Gln Leu Val Thr Glu
    425                 430                 435
```

```
cat gcg cag ctg gtg cag atc atc aag aag acg gag tcg gat gct gcg   1577
His Ala Gln Leu Val Gln Ile Ile Lys Lys Thr Glu Ser Asp Ala Ala
440                 445                 450                 455

ctg cac ccg cta ctg cag gag atc tac agg gac atg tac tgagttcctt    1626
Leu His Pro Leu Leu Gln Glu Ile Tyr Arg Asp Met Tyr
               460                 465

cagatcagcc acacctttc caggagttct gaagctgaca gcactacaaa ggagacgggg 1686

gagcagcacg attttgcaca aatatccacc actttaacct tagagcttgg acagtctgag 1746

ctgtaggtaa ccggcatatt attccatatc tttgttttaa ccagtacttc taagagcata 1806

gaactcaaat gctgggggag gtggctaatc tcaggactgg gaag                  1850



<210> 16
<211> 1609
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> (92)..(1606)

<400> 16
ttcaagtctt tttcttttaa cggattgatc ttttgctaga tagagacaaa atatcagtgt 60

gaattacagc aaacccctat tccatgctgt t atg ggt gaa act ctg gga gat    112
                                  Met Gly Glu Thr Leu Gly Asp
                                    1               5

tct cct att gac cca gaa agc gat tcc ttc act gat aca ctg tct gca   160
Ser Pro Ile Asp Pro Glu Ser Asp Ser Phe Thr Asp Thr Leu Ser Ala
         10                  15                  20                  \

aac ata tca caa gaa atg acc atg gtt gac aca gag atg cca ttc tgg   208
Asn Ile Ser Gln Glu Met Thr Met Val Asp Thr Glu Met Pro Phe Trp
     25                  30                  35

ccc acc aac ttt ggg atc agc tcc gtg gat ctc tcc gta atg gaa gac   256
Pro Thr Asn Phe Gly Ile Ser Ser Val Asp Leu Ser Val Met Glu Asp
 40                  45                  50                  55

cac tcc cac tcc ttt gat atc aag ccc ttc act act gtt gac ttc tcc   304
His Ser His Ser Phe Asp Ile Lys Pro Phe Thr Thr Val Asp Phe Ser
                 60                  65                  70

agc att tct act cca cat tac gaa gac att cca ttc aca aga aca gat   352
Ser Ile Ser Thr Pro His Tyr Glu Asp Ile Pro Phe Thr Arg Thr Asp
             75                  80                  85

cca gtg gtt gca gat tac aag tat gac ctg aaa ctt caa gag tac caa   400
Pro Val Val Ala Asp Tyr Lys Tyr Asp Leu Lys Leu Gln Glu Tyr Gln
         90                  95                  100
```

```
agt gca atc aaa gtg gag cct gca tct cca cct tat tat tct gag aag   448
Ser Ala Ile Lys Val Glu Pro Ala Ser Pro Pro Tyr Tyr Ser Glu Lys
    105                 110                 115

act cag ctc tac aat aag cct cat gaa gag cct tcc aac tcc ctc atg   496
Thr Gln Leu Tyr Asn Lys Pro His Glu Glu Pro Ser Asn Ser Leu Met
120                 125                 130                 135

gca att gaa tgt cgt gtc tgt gga gat aaa gct tct gga ttt cac tat   544
Ala Ile Glu Cys Arg Val Cys Gly Asp Lys Ala Ser Gly Phe His Tyr
                140                 145                 150

gga gtt cat gct tgt gaa gga tgc aag ggt ttc ttc cgg aga aca atc   592
Gly Val His Ala Cys Glu Gly Cys Lys Gly Phe Phe Arg Arg Thr Ile
            155                 160                 165

aga ttg aag ctt atc tat gac aga tgt gat ctt aac tgt cgg atc cac   640
Arg Leu Lys Leu Ile Tyr Asp Arg Cys Asp Leu Asn Cys Arg Ile His
        170                 175                 180

aaa aaa agt aga aat aaa tgt cag tac tgt cgg ttt cag aaa tgc ctt   688
Lys Lys Ser Arg Asn Lys Cys Gln Tyr Cys Arg Phe Gln Lys Cys Leu
    185                 190                 195

gca gtg ggg atg tct cat aat gcc atc agg ttt ggg cgg atg cca cag   736
Ala Val Gly Met Ser His Asn Ala Ile Arg Phe Gly Arg Met Pro Gln
200                 205                 210                 215

gcc gag aag gag aag ctg ttg gcg gag atc tcc agt gat atc gac cag   784
Ala Glu Lys Glu Lys Leu Leu Ala Glu Ile Ser Ser Asp Ile Asp Gln
                220                 225                 230

ctg aat cca gag tcc gct gac ctc cgg gcc ctg gca aaa cat ttg tat   832
Leu Asn Pro Glu Ser Ala Asp Leu Arg Ala Leu Ala Lys His Leu Tyr
            235                 240                 245

gac tca tac ata aag tcc ttc ccg ctg acc aaa gca aag gcg agg gcg   880
Asp Ser Tyr Ile Lys Ser Phe Pro Leu Thr Lys Ala Lys Ala Arg Ala
        250                 255                 260

atc ttg aca gga aag aca aca gac aaa tca cca ttc gtt atc tat gac   928
Ile Leu Thr Gly Lys Thr Thr Asp Lys Ser Pro Phe Val Ile Tyr Asp
    265                 270                 275

atg aat tcc tta atg atg gga gaa gat aaa atc aag ttc aaa cac atc   976
Met Asn Ser Leu Met Met Gly Glu Asp Lys Ile Lys Phe Lys His Ile
280                 285                 290                 295

acc ccc ctg cag gag cag agc aaa gag gtg gcc atc cgc atc ttt cag   1024
Thr Pro Leu Gln Glu Gln Ser Lys Glu Val Ala Ile Arg Ile Phe Gln
                300                 305                 310

ggc tgc cag ttt cgc tcc gtg gag gct gtg cag gag atc aca gag tat   1072
Gly Cys Gln Phe Arg Ser Val Glu Ala Val Gln Glu Ile Thr Glu Tyr
            315                 320                 325
```

```
gcc aaa agc att cct ggt ttt gta aat ctt gac ttg aac gac caa gta   1120
Ala Lys Ser Ile Pro Gly Phe Val Asn Leu Asp Leu Asn Asp Gln Val
        330                 335                 340

act ctc ctc aaa tat gga gtc cac gag atc att tac aca atg ctg gcc   1168
Thr Leu Leu Lys Tyr Gly Val His Glu Ile Ile Tyr Thr Met Leu Ala
    345                 350                 355

tcc ttg atg aat aaa gat ggg gtt ctc ata tcc gag ggc caa ggc ttc   1216
Ser Leu Met Asn Lys Asp Gly Val Leu Ile Ser Glu Gly Gln Gly Phe
360                 365                 370                 375

atg aca agg gag ttt cta aag agc ctg cga aag cct ttt ggt gac ttt   1264
Met Thr Arg Glu Phe Leu Lys Ser Leu Arg Lys Pro Phe Gly Asp Phe
                380                 385                 390

atg gag ccc aag ttt gag ttt gct gtg aag ttc aat gca ctg gaa tta   1312
Met Glu Pro Lys Phe Glu Phe Ala Val Lys Phe Asn Ala Leu Glu Leu
            395                 400                 405

gat gac agc gac ttg gca ata ttt att gct gtc att att ctc agt gga   1360
Asp Asp Ser Asp Leu Ala Ile Phe Ile Ala Val Ile Ile Leu Ser Gly
        410                 415                 420

gac cgc cca ggt ttg ctg aat gtg aag ccc att gaa gac att caa gac   1408
Asp Arg Pro Gly Leu Leu Asn Val Lys Pro Ile Glu Asp Ile Gln Asp
    425                 430                 435

aac ctg cta caa gcc ctg gag ctc cag ctg aag ctg aac cac cct gag   1456
Asn Leu Leu Gln Ala Leu Glu Leu Gln Leu Lys Leu Asn His Pro Glu
440                 445                 450                 455

tcc tca cag ctg ttt gcc aag ctg ctc cag aaa atg aca gac ctc aga   1504
Ser Ser Gln Leu Phe Ala Lys Leu Leu Gln Lys Met Thr Asp Leu Arg
                460                 465                 470

cag att gtc acg gaa cac gtg cag cta ctg cag gtg atc aag aag acg   1552
Gln Ile Val Thr Glu His Val Gln Leu Leu Gln Val Ile Lys Lys Thr
            475                 480                 485

gag aca gac atg agt ctt cac ccg ctc ctg cag gag atc tac aag gac   1600
Glu Thr Asp Met Ser Leu His Pro Leu Leu Gln Glu Ile Tyr Lys Asp
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ttg tac tag                                                      1609
Leu Tyr
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aagacagatg caccaacgag ggtctggaat ggtctggagt ggtctggaaa gcagggtcag 180

ataccccctgg aaaactgaag cccgtggagc aatgatctct acaggactgc ttcaaggctg 240

atgggaacca ccctgtagag gtccatctgc gttcagaccc agacgatgcc agagctatga 300

ctgggcctgc aggtgtggcg ccgaggggag atcagcc atg gag cag cca cag gag 355
Met Glu Gln Pro Gln Glu
1 5

gaa gcc cct gag gtc cgg gaa gag gag gag aaa gag gaa gtg gca gag 403
Glu Ala Pro Glu Val Arg Glu Glu Glu Glu Lys Glu Glu Val Ala Glu
10 15 20

gca gaa gga gcc cca gag ctc aat ggg gga cca cag cat gca ctt cct 451
Ala Glu Gly Ala Pro Glu Leu Asn Gly Gly Pro Gln His Ala Leu Pro
25 30 35

tcc agc agc tac aca gac ctc tcc cgg agc tcc tcg cca ccc tca ctg 499
Ser Ser Ser Tyr Thr Asp Leu Ser Arg Ser Ser Ser Pro Pro Ser Leu
40 45 50

ctg gac caa ctg cag atg ggc tgt gac ggg gcc tca tgc ggc agc ctc 547
Leu Asp Gln Leu Gln Met Gly Cys Asp Gly Ala Ser Cys Gly Ser Leu
55 60 65 70

aac atg gag tgc cgg gtg tgc ggg gac aag gca tcg ggc ttc cac tac 595
Asn Met Glu Cys Arg Val Cys Gly Asp Lys Ala Ser Gly Phe His Tyr
75 80 85

ggt gtt cat gca tgt gag ggg tgc aag ggc ttc ttc cgt cgt acg atc 643
Gly Val His Ala Cys Glu Gly Cys Lys Gly Phe Phe Arg Arg Thr Ile
90 95 100

cgc atg aag ctg gag tac gag aag tgt gag cgc agc tgc aag att cag 691
Arg Met Lys Leu Glu Tyr Glu Lys Cys Glu Arg Ser Cys Lys Ile Gln
105 110 115

aag aag aac cgc aac aag tgc cag tac tgc cgc ttc cag aag tgc ctg 739
Lys Lys Asn Arg Asn Lys Cys Gln Tyr Cys Arg Phe Gln Lys Cys Leu
120 125 130

gca ctg ggc atg tca cac aac gct atc cgt ttt ggt cgg atg ccg gag 787
Ala Leu Gly Met Ser His Asn Ala Ile Arg Phe Gly Arg Met Pro Glu
135 140 145 150

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gct gag aag agg aag ctg gtg gca ggg ctg act gca aac gag ggg agc   835
Ala Glu Lys Arg Lys Leu Val Ala Gly Leu Thr Ala Asn Glu Gly Ser
                155                 160                 165

cag tac aac cca cag gtg gcc gac ctg aag gcc ttc tcc aag cac atc   883
Gln Tyr Asn Pro Gln Val Ala Asp Leu Lys Ala Phe Ser Lys His Ile
            170                 175                 180

tac aat gcc tac ctg aaa aac ttc aac atg acc aaa aag aag gcc cgc   931
Tyr Asn Ala Tyr Leu Lys Asn Phe Asn Met Thr Lys Lys Lys Ala Arg
        185                 190                 195

agc atc ctc acc ggc aaa gcc agc cac acg gcg ccc ttt gtg atc cac   979
Ser Ile Leu Thr Gly Lys Ala Ser His Thr Ala Pro Phe Val Ile His
    200                 205                 210

gac atc gag aca ttg tgg cag gca gag aag ggg ctg gtg tgg aag cag   1027
Asp Ile Glu Thr Leu Trp Gln Ala Glu Lys Gly Leu Val Trp Lys Gln
215                 220                 225                 230

ttg gtg aat ggc ctg cct ccc tac aag gag atc agc gtg cac gtc ttc   1075
Leu Val Asn Gly Leu Pro Pro Tyr Lys Glu Ile Ser Val His Val Phe
                235                 240                 245

tac cgc tgc cag tgc acc aca gtg gag acc gtg cgg gag ctc act gag   1123
Tyr Arg Cys Gln Cys Thr Thr Val Glu Thr Val Arg Glu Leu Thr Glu
            250                 255                 260

ttc gcc aag agc atc ccc agc ttc agc agc ctc ttc ctc aac gac cag   1171
Phe Ala Lys Ser Ile Pro Ser Phe Ser Ser Leu Phe Leu Asn Asp Gln
        265                 270                 275

gtt acc ctt ctc aag tat ggc gtg cac gag gcc atc ttc gcc atg ctg   1219
Val Thr Leu Leu Lys Tyr Gly Val His Glu Ala Ile Phe Ala Met Leu
    280                 285                 290

gcc tct atc gtc aac aag gac ggg ctg ctg gta gcc aac ggc agt ggc   1267
Ala Ser Ile Val Asn Lys Asp Gly Leu Leu Val Ala Asn Gly Ser Gly
295                 300                 305                 310

ttt gtc acc cgt gag ttc ctg cgc agc ctc cgc aaa ccc ttc agt gat   1315
Phe Val Thr Arg Glu Phe Leu Arg Ser Leu Arg Lys Pro Phe Ser Asp
                315                 320                 325

atc att gag cct aag ttt gaa ttt gct gtc aag ttc aac gcc ctg gaa   1363
Ile Ile Glu Pro Lys Phe Glu Phe Ala Val Lys Phe Asn Ala Leu Glu
            330                 335                 340

ctt gat gac agt gac ctg gcc cta ttc att gcg gcc atc att ctg tgt   1411
Leu Asp Asp Ser Asp Leu Ala Leu Phe Ile Ala Ala Ile Ile Leu Cys
        345                 350                 355

gga gac cgg cca ggc ctc atg aac gtt cca cgg gtg gag gct atc cag   1459
Gly Asp Arg Pro Gly Leu Met Asn Val Pro Arg Val Glu Ala Ile Gln
    360                 365                 370
```

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gac acc atc ctg cgt gcc ctc gaa ttc cac ctg cag gcc aac cac cct   1507
Asp Thr Ile Leu Arg Ala Leu Glu Phe His Leu Gln Ala Asn His Pro
375                 380                 385                 390

gat gcc cag tac ctc ttc ccc aag ctg ctg cag aag atg gct gac ctg   1555
Asp Ala Gln Tyr Leu Phe Pro Lys Leu Leu Gln Lys Met Ala Asp Leu
                395                 400                 405

cgg caa ctg gtc acc gag cac gcc cag atg atg cag cgg atc aag aag   1603
Arg Gln Leu Val Thr Glu His Ala Gln Met Met Gln Arg Ile Lys Lys
            410                 415                 420

acc gaa acc gag acc tcg ctg cac cct ctg ctc cag gag atc tac aag   1651
Thr Glu Thr Glu Thr Ser Leu His Pro Leu Leu Gln Glu Ile Tyr Lys
        425                 430                 435

gac atg tac taacggcggc acccaggcct ccctgcagac tccaatgggg           1700
Asp Met Tyr
    440

ccagcactgg aggggcccac ccacatgact tttccattga ccagctctct tcctgtcttt 1760

gttgtctccc tctttctcag ttcctctttc ttttctaatt cctgttgctc tgtttcttcc 1820

tttctgtagg tttctctctt cccttctccc ttctcccttg ccctcccttt ctctctccta 1880

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gacacccagt gtccttccat cttcacactg gtttgccagg ccaatgttgc tgatggcccc 2360

tccagcacac acacataagc actgaaatca ctttacctgc aggcaccatg cacctccctt 2420

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ggccaggtct ccggggaggc aggggtcctg caggtcctgg tgggtcagcc cagcacctcg 2540

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tacagctctt ctcagtgtct gaacaatctc caaaattgaa atgtatattt ttgctaggag 3200

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ccagctcctt tcgcccgcgc cctccgttcg ctccggacac c atg gac aag ttt tgg 176
Met Asp Lys Phe Trp
1 5

tgg cac gca gcc tgg gga ctc tgc ctc gtg ccg ctg agc ctg gcg cag 224
Trp His Ala Ala Trp Gly Leu Cys Leu Val Pro Leu Ser Leu Ala Gln
10 15 20

atc gat ttg aat ata acc tgc cgc ttt gca ggt gta ttc cac gtg gag 272
Ile Asp Leu Asn Ile Thr Cys Arg Phe Ala Gly Val Phe His Val Glu
25 30 35

aaa aat ggt cgc tac agc atc tct cgg acg gag gcc gct gac ctc tgc 320
Lys Asn Gly Arg Tyr Ser Ile Ser Arg Thr Glu Ala Ala Asp Leu Cys
40 45 50

aag gct ttc aat agc acc ttg ccc aca atg gcc cag atg gag aaa gct 368
Lys Ala Phe Asn Ser Thr Leu Pro Thr Met Ala Gln Met Glu Lys Ala
55 60 65

ctg agc atc gga ttt gag acc tgc agg tat ggg ttc ata gaa ggg cac 416
Leu Ser Ile Gly Phe Glu Thr Cys Arg Tyr Gly Phe Ile Glu Gly His
70 75 80 85

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gtg gtg att ccc cgg atc cac ccc aac tcc atc tgt gca gca aac aac   464
Val Val Ile Pro Arg Ile His Pro Asn Ser Ile Cys Ala Ala Asn Asn
                 90                  95                 100

aca ggg gtg tac atc ctc aca tcc aac acc tcc cag tat gac aca tat   512
Thr Gly Val Tyr Ile Leu Thr Ser Asn Thr Ser Gln Tyr Asp Thr Tyr
            105                 110                 115

tgc ttc aat gct tca gct cca cct gaa gaa gat tgt aca tca gtc aca   560
Cys Phe Asn Ala Ser Ala Pro Pro Glu Glu Asp Cys Thr Ser Val Thr
        120                 125                 130

gac ctg ccc aat gcc ttt gat gga cca att acc ata act att gtt aac   608
Asp Leu Pro Asn Ala Phe Asp Gly Pro Ile Thr Ile Thr Ile Val Asn
    135                 140                 145

cgt gat ggc acc cgc tat gtc cag aaa gga gaa tac aga acg aat cct   656
Arg Asp Gly Thr Arg Tyr Val Gln Lys Gly Glu Tyr Arg Thr Asn Pro
150                 155                 160                 165

gaa gac atc tac ccc agc aac cct act gat gat gac gtg agc agc ggc   704
Glu Asp Ile Tyr Pro Ser Asn Pro Thr Asp Asp Asp Val Ser Ser Gly
                170                 175                 180

tcc tcc agt gaa agg agc agc act tca gga ggt tac atc ttt tac acc   752
Ser Ser Ser Glu Arg Ser Ser Thr Ser Gly Gly Tyr Ile Phe Tyr Thr
            185                 190                 195

ttt tct act gta cac ccc atc cca gac gaa gac agt ccc tgg atc acc   800
Phe Ser Thr Val His Pro Ile Pro Asp Glu Asp Ser Pro Trp Ile Thr
        200                 205                 210

gac agc aca gac aga atc cct gct acc act ttg atg agc act agt gct   848
Asp Ser Thr Asp Arg Ile Pro Ala Thr Thr Leu Met Ser Thr Ser Ala
    215                 220                 225

aca gca act gag aca gca acc aag agg caa gaa acc tgg gat tgg ttt   896
Thr Ala Thr Glu Thr Ala Thr Lys Arg Gln Glu Thr Trp Asp Trp Phe
230                 235                 240                 245

tca tgg ttg ttt cta cca tca gag tca aag aat cat ctt cac aca aca   944
Ser Trp Leu Phe Leu Pro Ser Glu Ser Lys Asn His Leu His Thr Thr
                250                 255                 260

aca caa atg gct ggt acg tct tca aat acc atc tca gca ggc tgg gag   992
Thr Gln Met Ala Gly Thr Ser Ser Asn Thr Ile Ser Ala Gly Trp Glu
            265                 270                 275

cca aat gaa gaa aat gaa gat gaa aga gac aga cac ctc agt ttt tct   1040
Pro Asn Glu Glu Asn Glu Asp Glu Arg Asp Arg His Leu Ser Phe Ser
        280                 285                 290

gga tca ggc att gat gat gat gaa gat ttt atc tcc agc acc att tca   1088
Gly Ser Gly Ile Asp Asp Asp Glu Asp Phe Ile Ser Ser Thr Ile Ser
    295                 300                 305
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acc aca cca cgg gct ttt gac cac aca aaa cag aac cag gac tgg acc   1136
Thr Thr Pro Arg Ala Phe Asp His Thr Lys Gln Asn Gln Asp Trp Thr
310                 315                 320                 325

cag tgg aac cca agc cat tca aat ccg gaa gtg cta ctt cag aca acc   1184
Gln Trp Asn Pro Ser His Ser Asn Pro Glu Val Leu Leu Gln Thr Thr
                330                 335                 340

aca agg atg act gat gta gac aga aat ggc acc act gct tat gaa gga   1232
Thr Arg Met Thr Asp Val Asp Arg Asn Gly Thr Thr Ala Tyr Glu Gly
            345                 350                 355

aac tgg aac cca gaa gca cac cct ccc ctc att cac cat gag cat cat   1280
Asn Trp Asn Pro Glu Ala His Pro Pro Leu Ile His His Glu His His
        360                 365                 370

gag gaa gaa gag acc cca cat tct aca agc aca atc cag gca act cct   1328
Glu Glu Glu Glu Thr Pro His Ser Thr Ser Thr Ile Gln Ala Thr Pro
    375                 380                 385

agt agt aca acg gaa gaa aca gct acc cag aag gaa cag tgg ttt ggc   1376
Ser Ser Thr Thr Glu Glu Thr Ala Thr Gln Lys Glu Gln Trp Phe Gly
390                 395                 400                 405

aac aga tgg cat gag gga tat cgc caa aca ccc aaa gaa gac tcc cat   1424
Asn Arg Trp His Glu Gly Tyr Arg Gln Thr Pro Lys Glu Asp Ser His
                410                 415                 420

tcg aca aca ggg aca gct gca gcc tca gct cat acc agc cat cca atg   1472
Ser Thr Thr Gly Thr Ala Ala Ala Ser Ala His Thr Ser His Pro Met
            425                 430                 435

caa gga agg aca aca cca agc cca gag gac agt tcc tgg act gat ttc   1520
Gln Gly Arg Thr Thr Pro Ser Pro Glu Asp Ser Ser Trp Thr Asp Phe
        440                 445                 450

ttc aac cca atc tca cac ccc atg gga cga ggt cat caa gca gga aga   1568
Phe Asn Pro Ile Ser His Pro Met Gly Arg Gly His Gln Ala Gly Arg
    455                 460                 465

agg atg gat atg gac tcc agt cat agt ata acg ctt cag cct act gca   1616
Arg Met Asp Met Asp Ser Ser His Ser Ile Thr Leu Gln Pro Thr Ala
470                 475                 480                 485

aat cca aac aca ggt ttg gtg gaa gat ttg gac agg aca gga cct ctt   1664
Asn Pro Asn Thr Gly Leu Val Glu Asp Leu Asp Arg Thr Gly Pro Leu
                490                 495                 500

tca atg aca acg cag cag agt aat tct cag agc ttc tct aca tca cat   1712
Ser Met Thr Thr Gln Gln Ser Asn Ser Gln Ser Phe Ser Thr Ser His
            505                 510                 515

gaa ggc ttg gaa gaa gat aaa gac cat cca aca act tct act ctg aca   1760
Glu Gly Leu Glu Glu Asp Lys Asp His Pro Thr Thr Ser Thr Leu Thr
        520                 525                 530
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tca agc aat agg aat gat gtc aca ggt gga aga aga gac cca aat cat   1808
Ser Ser Asn Arg Asn Asp Val Thr Gly Gly Arg Arg Asp Pro Asn His
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tct gaa ggc tca act act tta ctg gaa ggt tat acc tct cat tac cca   1856
Ser Glu Gly Ser Thr Thr Leu Leu Glu Gly Tyr Thr Ser His Tyr Pro
550                 555                 560                 565

cac acg aag gaa agc agg acc ttc atc cca gtg acc tca gct aag act   1904
His Thr Lys Glu Ser Arg Thr Phe Ile Pro Val Thr Ser Ala Lys Thr
                570                 575                 580

ggg tcc ttt gga gtt act gca gtt act gtt gga gat tcc aac tct aat   1952
Gly Ser Phe Gly Val Thr Ala Val Thr Val Gly Asp Ser Asn Ser Asn
            585                 590                 595

gtc aat cgt tcc tta tca gga gac caa gac aca ttc cac ccc agt ggg   2000
Val Asn Arg Ser Leu Ser Gly Asp Gln Asp Thr Phe His Pro Ser Gly
        600                 605                 610

ggg tcc cat acc act cat gga tct gaa tca gat gga cac tca cat ggg   2048
Gly Ser His Thr Thr His Gly Ser Glu Ser Asp Gly His Ser His Gly
    615                 620                 625

agt caa gaa ggt gga gca aac aca acc tct ggt cct ata agg aca ccc   2096
Ser Gln Glu Gly Gly Ala Asn Thr Thr Ser Gly Pro Ile Arg Thr Pro
630                 635                 640                 645

caa att cca gaa tgg ctg atc atc ttg gca tcc ctc ttg gcc ttg gct   2144
Gln Ile Pro Glu Trp Leu Ile Ile Leu Ala Ser Leu Leu Ala Leu Ala
                650                 655                 660

ttg att ctt gca gtt tgc att gca gtc aac agt cga aga agg tgt ggg   2192
Leu Ile Leu Ala Val Cys Ile Ala Val Asn Ser Arg Arg Arg Cys Gly
            665                 670                 675

cag aag aaa aag cta gtg atc aac agt ggc aat gga gct gtg gag gac   2240
Gln Lys Lys Lys Leu Val Ile Asn Ser Gly Asn Gly Ala Val Glu Asp
        680                 685                 690

aga aag cca agt gga ctc aac gga gag gcc agc aag tct cag gaa atg   2288
Arg Lys Pro Ser Gly Leu Asn Gly Glu Ala Ser Lys Ser Gln Glu Met
    695                 700                 705

gtg cat ttg gtg aac aag gag tcg tca gaa act cca gac cag ttt atg   2336
Val His Leu Val Asn Lys Glu Ser Ser Glu Thr Pro Asp Gln Phe Met
710                 715                 720                 725

aca gct gat gag aca agg aac ctg cag aat gtg gac atg aag att ggg   2384
Thr Ala Asp Glu Thr Arg Asn Leu Gln Asn Val Asp Met Lys Ile Gly
                730                 735                 740

gtg taacacctac accattatct tggaaagaaa caaccgttgg aaacataacc        2437
Val

attacaggga gctgggacac ttaacagatg caatgtgcta ctgattgttt cattgcgaat 2497

ctttttagc ataaaatttt ctactctttt tgtttttgt gttttgttct ttaaagtcag 2557
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aatttgatcg ttccagttcc cacttggagg cctttcatcc ctcgggtgtg ctatggatgg 2677

cttctaacaa aaactacaca tatgtattcc tgatcgccaa cctttccccc accagctaag 2737

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ccctggatca gtcctttgat cagtataatt ttttaaagtt actttgtcag aggcacaaaa 3037

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attccggccc caactgcacc atccctggcc tgtggacctg gctccggaat tcactgcggc 240

ccagcccctc tttcacccac ttcctgctca ctcacgggcg ctggttctgg gagtttgtca 300

atgccacctt catccgagag atg ctc atg cgc ctg gta ctc aca gtg cgc tcc 353
Met Leu Met Arg Leu Val Leu Thr Val Arg Ser
1 5 10

aac ctt atc ccc agt ccc ccc acc tac aac tca gca cat gac tac atc 401
Asn Leu Ile Pro Ser Pro Pro Thr Tyr Asn Ser Ala His Asp Tyr Ile
15 20 25

agc tgg gag tct ttc tcc aac gtg agc tat tac act cgt att ctg ccc 449
Ser Trp Glu Ser Phe Ser Asn Val Ser Tyr Tyr Thr Arg Ile Leu Pro
30 35 40

tct gtg cct aaa gat tgc ccc aca ccc atg gga acc aaa ggg aag aag 497
Ser Val Pro Lys Asp Cys Pro Thr Pro Met Gly Thr Lys Gly Lys Lys
45 50 55

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cag ttg cca gat gcc cag ctc ctg gcc cgc cgc ttc ctg ctc agg agg   545
Gln Leu Pro Asp Ala Gln Leu Leu Ala Arg Arg Phe Leu Leu Arg Arg
 60                  65                  70                  75

aag ttc ata cct gac ccc caa ggc acc aac ctc atg ttt gcc ttc ttt   593
Lys Phe Ile Pro Asp Pro Gln Gly Thr Asn Leu Met Phe Ala Phe Phe
                 80                  85                  90

gca caa cac ttc acc cac cag ttc ttc aaa act tct ggc aag atg ggt   641
Ala Gln His Phe Thr His Gln Phe Phe Lys Thr Ser Gly Lys Met Gly
            95                 100                 105

cct ggc ttc acc aag gcc ttg ggc cat ggg gta gac ctc ggc cac att   689
Pro Gly Phe Thr Lys Ala Leu Gly His Gly Val Asp Leu Gly His Ile
        110                 115                 120

tat gga gac aat ctg gag cgt cag tat caa ctg cgg ctc ttt aag gat   737
Tyr Gly Asp Asn Leu Glu Arg Gln Tyr Gln Leu Arg Leu Phe Lys Asp
    125                 130                 135

ggg aaa ctc aag tac cag gtg ctg gat gga gaa atg tac ccg ccc tcg   785
Gly Lys Leu Lys Tyr Gln Val Leu Asp Gly Glu Met Tyr Pro Pro Ser
140                 145                 150                 155

gta gaa gag gcg cct gtg ttg atg cac tac ccc cga ggc atc ccg ccc   833
Val Glu Glu Ala Pro Val Leu Met His Tyr Pro Arg Gly Ile Pro Pro
                160                 165                 170

cag agc cag atg gct gtg ggc cag gag gtg ttt ggg ctg ctt cct ggg   881
Gln Ser Gln Met Ala Val Gly Gln Glu Val Phe Gly Leu Leu Pro Gly
            175                 180                 185

ctc atg ctg tat gcc acg ctc tgg cta cgt gag cac aac cgt gtg tgt   929
Leu Met Leu Tyr Ala Thr Leu Trp Leu Arg Glu His Asn Arg Val Cys
        190                 195                 200

gac ctg ctg aag gct gag cac ccc acc tgg ggc gat gag cag ctt ttc   977
Asp Leu Leu Lys Ala Glu His Pro Thr Trp Gly Asp Glu Gln Leu Phe
    205                 210                 215

cag acg acc cgc ctc atc ctc ata ggg gag acc atc aag att gtc atc   1025
Gln Thr Thr Arg Leu Ile Leu Ile Gly Glu Thr Ile Lys Ile Val Ile
220                 225                 230                 235

gag gag tac gtg cag cag ctg agt ggc tat ttc ctg cag ctg aaa ttt   1073
Glu Glu Tyr Val Gln Gln Leu Ser Gly Tyr Phe Leu Gln Leu Lys Phe
                240                 245                 250

gac cca gag ctg ctg ttc ggt gtc cag ttc caa tac cgc aac cgc att   1121
Asp Pro Glu Leu Leu Phe Gly Val Gln Phe Gln Tyr Arg Asn Arg Ile
            255                 260                 265

gcc atg gag ttc aac cat ctc tac cac tgg cac ccc ctc atg cct gac   1169
Ala Met Glu Phe Asn His Leu Tyr His Trp His Pro Leu Met Pro Asp
        270                 275                 280
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tcc ttc aag gtg ggc tcc cag gag tac agc tac gag cag ttc ttg ttc   1217
Ser Phe Lys Val Gly Ser Gln Glu Tyr Ser Tyr Glu Gln Phe Leu Phe
    285                 290                 295

aac acc tcc atg ttg gtg gac tat ggg gtt gag gcc ctg gtg gat gcc   1265
Asn Thr Ser Met Leu Val Asp Tyr Gly Val Glu Ala Leu Val Asp Ala
300                 305                 310                 315

ttc tct cgc cag att gct ggc cgg atc ggt ggg ggc agg aac atg gac   1313
Phe Ser Arg Gln Ile Ala Gly Arg Ile Gly Gly Gly Arg Asn Met Asp
                320                 325                 330

cac cac atc ctg cat gtg gct gtg gat gtc atc agg gag tct cgg gag   1361
His His Ile Leu His Val Ala Val Asp Val Ile Arg Glu Ser Arg Glu
            335                 340                 345

atg cgg ctg cag ccc ttc aat gag tac cgc aag agg ttt ggc atg aaa   1409
Met Arg Leu Gln Pro Phe Asn Glu Tyr Arg Lys Arg Phe Gly Met Lys
        350                 355                 360

ccc tac acc tcc ttc cag gag ctc gta gga gag aag gag atg gca gca   1457
Pro Tyr Thr Ser Phe Gln Glu Leu Val Gly Glu Lys Glu Met Ala Ala
    365                 370                 375

gag ttg gag gaa ttg tat gga gac att gat gcg ttg gag ttc tac cct   1505
Glu Leu Glu Glu Leu Tyr Gly Asp Ile Asp Ala Leu Glu Phe Tyr Pro
380                 385                 390                 395

gga ctg ctt ctt gaa aag tgc cat cca aac tct atc ttt ggg gag agt   1553
Gly Leu Leu Leu Glu Lys Cys His Pro Asn Ser Ile Phe Gly Glu Ser
                400                 405                 410

atg ata gag att ggg gct ccc ttt tcc ctc aag ggt ctc cta ggg aat   1601
Met Ile Glu Ile Gly Ala Pro Phe Ser Leu Lys Gly Leu Leu Gly Asn
            415                 420                 425

ccc atc tgt tct ccg gag tac tgg aag ccg agc aca ttt ggc ggc gag   1649
Pro Ile Cys Ser Pro Glu Tyr Trp Lys Pro Ser Thr Phe Gly Gly Glu
        430                 435                 440

gtg ggc ttt aac att gtc aag acg gcc aca ctg aag aag ctg gtc tgc   1697
Val Gly Phe Asn Ile Val Lys Thr Ala Thr Leu Lys Lys Leu Val Cys
    445                 450                 455

ctc aac acc aag acc tgt ccc tac gtt tcc ttc cgt gtg ccg gat gcc   1745
Leu Asn Thr Lys Thr Cys Pro Tyr Val Ser Phe Arg Val Pro Asp Ala
460                 465                 470                 475

agt cag gat gat ggg cct gct gtg gag cga cca tcc aca gag           1787
Ser Gln Asp Asp Gly Pro Ala Val Glu Arg Pro Ser Thr Glu
                480                 485

ctctgagggg caggaaagca gcattctgga ggggagagct ttgtgcttgt cattccagag 1847

tgctgaggcc agggctgatg gtcttaaatg ctcattttct ggtttggcat ggtgagtgtt 1907

ggggttgaca tttagaactt taagtctcac ccattatctg gaatattgtg attctgttta 1967
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ttcttccaga atgctgaact ccttgttagc ccttcagatt gttaggagtg gttctcattt 2027

ggtctgccag aatactgggt tcttagttga caacctagaa tgtcagattt ctggttgatt 2087

tgtaacacag tcattctagg atgtggagct actgatgaaa tctgctagaa agttaggggg 2147

ttcttatttt gcattccaga atcttgactt tctgattggt gattcaaagt gttgtgttcc 2207

tggctgatga tccagaacag tggctcgtat cccaaatctg tcagcatctg gctgtctaga 2267

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tcttcttggg acccccacta agaccctggt ctgaggatgt agagagaaca ggtgggctgt 2447

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cagctgtttc tcatgaagct aataaaattc gc 2539

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ctcagcgccc agcaccgccg ctcccggcaa cccggagcgc gcaccgcagc cggcggccga 180

gctcgcgcat cccagccatc actcttccac ctgctcctta gagaagggaa g atg agt 237
Met Ser
1

gag tcg agc tcg aag tcc agc cag ccc ttg gcc tcc aag cag gaa aag 285
Glu Ser Ser Ser Lys Ser Ser Gln Pro Leu Ala Ser Lys Gln Glu Lys
5 10 15

gac ggc act gag aag cgg ggc cgg ggc agg ccg cgc aag cag cct ccg 333
Asp Gly Thr Glu Lys Arg Gly Arg Gly Arg Pro Arg Lys Gln Pro Pro
20 25 30

aag gag ccc agc gaa gtg cca aca cct aag aga cct cgg ggc cga cca 381
Lys Glu Pro Ser Glu Val Pro Thr Pro Lys Arg Pro Arg Gly Arg Pro
35 40 45 50

aag gga agc aaa aac aag ggt gct gcc aag acc cgg aaa acc acc aca 429
Lys Gly Ser Lys Asn Lys Gly Ala Ala Lys Thr Arg Lys Thr Thr Thr
55 60 65

act cca gga agg aaa cca agg ggc aga ccc aaa aaa ctg gag aag gag 477
Thr Pro Gly Arg Lys Pro Arg Gly Arg Pro Lys Lys Leu Glu Lys Glu
70 75 80

gaa gag gag ggc atc tcg cag gag tcc tcg gag gag gag cag 519
Glu Glu Glu Gly Ile Ser Gln Glu Ser Ser Glu Glu Glu Gln
85 90 95

tgacccatgc gtgccgcctg ctcctcactg gaggagcagc ttccttctgg gactggacag 579

ctttgctccg ctcccaccgc ccccgccccc tccccaggcc caccatcacc accgcctctg 639

gccgccaccc ccatcttcca cctgtgccct caccaccaca ctacacagca caccagccgc 699

tgcagggctc ccatgggctg agtggggagc agttttcccc tggcctcagt tcccagctcc 759

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gcaccctgca cctgctgcgt ccccactccc ttggtggtgg ggacattgct ctctgggctt 879

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tccctagtcc ccgtactagg ttggacagcc cccttcggct acaggaaggc aggaggggtg 1179

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tggccgccac ctgaggtggg ctggggctgc tcccctaacc ctactttgct tccgccactc 1359

agccatttcc ccctcctcag atggggcacc aataacaagg agctcaccct gcccgctccc 1419

aaccccccctc ctgctcctcc ctgcccccca aggttctggt tccatttttc ctctgttcac 1479

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attgctgctg ctaccagcgc caaatgttca tcctcattgc ctcctgttct gcccacgatc 1599

ccctccccca agatactctt tgtggggaag aggggctggg gcatggcagg ctgggtgacc 1659

gactacccca gtcccaggga aggtgccctg cccctaggat gctgcagcag agtgagcaag 1719

ggggcccgaa tcgaccataa agggtgtagg ggccacctcc tccccctgtt ctgttgggga 1779

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Met Ala His Lys Gln Ile
1 5

tac tac tcg gac aag tac ttc gac gaa cac tac gag tac cgg cat gtt 161
Tyr Tyr Ser Asp Lys Tyr Phe Asp Glu His Tyr Glu Tyr Arg His Val
10 15 20

atg tta ccc aga gaa ctt tcc aaa caa gta cct aaa act cat ctg atg 209
Met Leu Pro Arg Glu Leu Ser Lys Gln Val Pro Lys Thr His Leu Met
25 30 35

tct gaa gag gag tgg agg aga ctt ggt gtc caa cag agt cta ggc tgg 257
Ser Glu Glu Glu Trp Arg Arg Leu Gly Val Gln Gln Ser Leu Gly Trp
40 45 50

gtt cat tac atg att cat gag cca gaa cca cat att ctt ctc ttt aga 305
Val His Tyr Met Ile His Glu Pro Glu Pro His Ile Leu Leu Phe Arg
55 60 65 70

cga cct ctt cca aaa gat caa caa aaa tgaagtttat ctggggatcg 352
Arg Pro Leu Pro Lys Asp Gln Gln Lys
75

tcaaatcttt ttcaaattta atgtatatgt gtatataagg tagtattcag tgaatacttg 412

agaaatgtac aaatctttca tccatacctg tgcatgagct gtattcttca cagcaacaga 472

gctcagttaa atgcaactgc aagtaggtta ctgtaagatg tttaagataa aagttcttcc 532

agtcagtttt tctcttaagt gcctgtttga gtttactgaa acagtttact tttgttcaat 592

aaagtttgta tgttgcattt aaaaaaaaaa aaaa 626

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<213> Homo sapiens

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tccgtcccgt ccaccgtccg cagctggtag ccagcctgcc cctcgcctcg actccctttc 120

accaacaccg acacccacat tgacacctcc agtccggcca gccgctccac tcgttgcctt 180

tgcatctcca cacatggcgt cctcgcgcag agcggcggct cctccggggg acccgcggtc 240

cccaccgtgc agcggggcat catcaag atg gtc ctc tca ggg tgc gcc atc att 294
Met Val Leu Ser Gly Cys Ala Ile Ile
1 5

gtc cga ggt cag cct cgt ggt ggg cct cct cct gag cgg cag atc aac 342
Val Arg Gly Gln Pro Arg Gly Gly Pro Pro Pro Glu Arg Gln Ile Asn
10 15 20 25

ctc agc aac att cgt gct gga aat ctt gct cgc cgg gca gcc gcc aca 390
Leu Ser Asn Ile Arg Ala Gly Asn Leu Ala Arg Arg Ala Ala Ala Thr
30 35 40

caa cct gat gca aag gat acc cct gat gag ccc tgg gca ttt cca gct 438
Gln Pro Asp Ala Lys Asp Thr Pro Asp Glu Pro Trp Ala Phe Pro Ala
45 50 55

cga gag ttc ctt cga aag aag ctg att ggg aag gaa gtc tgt ttc acg 486
Arg Glu Phe Leu Arg Lys Lys Leu Ile Gly Lys Glu Val Cys Phe Thr
60 65 70

ata gaa aac aag act ccc cag ggg cga gag tat ggc atg atc tac ctt 534
Ile Glu Asn Lys Thr Pro Gln Gly Arg Glu Tyr Gly Met Ile Tyr Leu
75 80 85

gga aaa gat acc aat ggg gaa aac att gca gaa tca ctg gtt gca gag 582
Gly Lys Asp Thr Asn Gly Glu Asn Ile Ala Glu Ser Leu Val Ala Glu
90 95 100 105

ggc tta gcc acc cgg aga gaa ggc atg aga gct aat aat cct gag cag 630
Gly Leu Ala Thr Arg Arg Glu Gly Met Arg Ala Asn Asn Pro Glu Gln
110 115 120

aac cgg ctt tca gaa tgt gaa gaa caa gca aag gca gcc aag aaa ggg 678
Asn Arg Leu Ser Glu Cys Glu Glu Gln Ala Lys Ala Ala Lys Lys Gly
125 130 135

atg tgg agt gag ggg aac ggt tca cat act atc cgg gat ctc aag tat 726
Met Trp Ser Glu Gly Asn Gly Ser His Thr Ile Arg Asp Leu Lys Tyr
140 145 150

acc att gaa aac cca agg cac ttt gtg gac tca cac cac cag aag cct 774
Thr Ile Glu Asn Pro Arg His Phe Val Asp Ser His His Gln Lys Pro
155 160 165

gtt aat gct atc atc gag cat gtg cgg gac ggc agt gtg gtc agg gcc 822
Val Asn Ala Ile Ile Glu His Val Arg Asp Gly Ser Val Val Arg Ala
170 175 180 185

```
ctg ctc ctc cca gat tac tac ctg gtt aca gtc atg ctg tca ggc atc   870
Leu Leu Leu Pro Asp Tyr Tyr Leu Val Thr Val Met Leu Ser Gly Ile
                190                 195                 200

aag tgc cca act ttt cga cgg gaa gca gat ggc agt gaa act cca gag   918
Lys Cys Pro Thr Phe Arg Arg Glu Ala Asp Gly Ser Glu Thr Pro Glu
            205                 210                 215

cct ttt gct gca gaa gcc aaa ttt ttc act gag tcg cga ctg ctt cag   966
Pro Phe Ala Ala Glu Ala Lys Phe Phe Thr Glu Ser Arg Leu Leu Gln
        220                 225                 230

aga gat gtt cag atc att ctg gag agc tgc cac aac cag aac att gtg   1014
Arg Asp Val Gln Ile Ile Leu Glu Ser Cys His Asn Gln Asn Ile Val
    235                 240                 245

ggt acc atc ctt cat cca aat ggc aac atc aca gag ctc ctc ctg aag   1062
Gly Thr Ile Leu His Pro Asn Gly Asn Ile Thr Glu Leu Leu Leu Lys
250                 255                 260                 265

gaa ggt ttc gca cgc tgt gtg gac tgg tcg att gca gtt tac acc cgg   1110
Glu Gly Phe Ala Arg Cys Val Asp Trp Ser Ile Ala Val Tyr Thr Arg
                270                 275                 280

ggc gca gaa aag ctg agg gcg gca gag agg ttt gcc aaa gag cgc agg   1158
Gly Ala Glu Lys Leu Arg Ala Ala Glu Arg Phe Ala Lys Glu Arg Arg
            285                 290                 295

ctg aga ata tgg aga gac tat gtg gct ccc aca gct aat ttg gac caa   1206
Leu Arg Ile Trp Arg Asp Tyr Val Ala Pro Thr Ala Asn Leu Asp Gln
        300                 305                 310

aag gac aag cag ttt gtt gcc aag gtg atg cag gtt ctg aat gct gat   1254
Lys Asp Lys Gln Phe Val Ala Lys Val Met Gln Val Leu Asn Ala Asp
    315                 320                 325

gcc att gtt gtg aag ctg aac tca ggc gat tac aag acg att cac ctg   1302
Ala Ile Val Val Lys Leu Asn Ser Gly Asp Tyr Lys Thr Ile His Leu
330                 335                 340                 345

tcc agc atc cga cca ccg agg ctg gag ggg gag aac acc cag gat aag   1350
Ser Ser Ile Arg Pro Pro Arg Leu Glu Gly Glu Asn Thr Gln Asp Lys
                350                 355                 360

aac aag aaa ctg cgt ccc ctg tat gac att cct tac atg ttt gag gcc   1398
Asn Lys Lys Leu Arg Pro Leu Tyr Asp Ile Pro Tyr Met Phe Glu Ala
            365                 370                 375

cgg gaa ttt ctt cga aaa aag ctt att ggg aag aag gtc aat gtg acg   1446
Arg Glu Phe Leu Arg Lys Lys Leu Ile Gly Lys Lys Val Asn Val Thr
        380                 385                 390

gtg gac tac att aga cca gcc agc cca gcc aca gag aca gtg cct gcc   1494
Val Asp Tyr Ile Arg Pro Ala Ser Pro Ala Thr Glu Thr Val Pro Ala
    395                 400                 405
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ttt tca gag cgt acc tgt gcc act gtc acc att gga gga ata aac att   1542
Phe Ser Glu Arg Thr Cys Ala Thr Val Thr Ile Gly Gly Ile Asn Ile
410                 415                 420                 425

gct gag gct ctt gtc agc aaa ggt cta gcc aca gtg atc aga tac cgg   1590
Ala Glu Ala Leu Val Ser Lys Gly Leu Ala Thr Val Ile Arg Tyr Arg
                430                 435                 440

cag gat gat gac cag aga tca tca cac tac gat gaa ctg ctt gct gca   1638
Gln Asp Asp Asp Gln Arg Ser Ser His Tyr Asp Glu Leu Leu Ala Ala
            445                 450                 455

gag gcc aga gct att aag aat ggc aaa gga ttg cat agc aag aag gaa   1686
Glu Ala Arg Ala Ile Lys Asn Gly Lys Gly Leu His Ser Lys Lys Glu
        460                 465                 470

gtg cct atc cac cgt gtt gca gat ata tct ggg gat acc caa aaa gca   1734
Val Pro Ile His Arg Val Ala Asp Ile Ser Gly Asp Thr Gln Lys Ala
    475                 480                 485

aag cag ttc ctg cct ttt ctt cag cgg gca ggt cgt tct gaa gct gtg   1782
Lys Gln Phe Leu Pro Phe Leu Gln Arg Ala Gly Arg Ser Glu Ala Val
490                 495                 500                 505

gtg gaa tac gtc ttc agt ggt tct cgt ctc aaa ctc tat ttg cca aag   1830
Val Glu Tyr Val Phe Ser Gly Ser Arg Leu Lys Leu Tyr Leu Pro Lys
                510                 515                 520

gaa act tgc ctt atc acc ttc ttg ctt gca ggc att gaa tgc ccc aga   1878
Glu Thr Cys Leu Ile Thr Phe Leu Leu Ala Gly Ile Glu Cys Pro Arg
            525                 530                 535

gga gcc cga aac ctc cca ggc ttg gtg cag gaa gga gag ccc ttc agc   1926
Gly Ala Arg Asn Leu Pro Gly Leu Val Gln Glu Gly Glu Pro Phe Ser
        540                 545                 550

gag gaa gct aca ctt ttc acc aag gaa ctg gtg ctg cag cga gag gtg   1974
Glu Glu Ala Thr Leu Phe Thr Lys Glu Leu Val Leu Gln Arg Glu Val
    555                 560                 565

gag gtg gag gtg gag agc atg gac aag gcc ggc aac ttt atc ggc tgg   2022
Glu Val Glu Val Glu Ser Met Asp Lys Ala Gly Asn Phe Ile Gly Trp
570                 575                 580                 585

ctg cac atc gac ggt gcc aac ctg tcc gtc ctg ctg gtg gag cac gcg   2070
Leu His Ile Asp Gly Ala Asn Leu Ser Val Leu Leu Val Glu His Ala
                590                 595                 600

ctc tcc aag gtc cac ttc acc gcc gaa cgc agc tcc tac tac aag tcc   2118
Leu Ser Lys Val His Phe Thr Ala Glu Arg Ser Ser Tyr Tyr Lys Ser
            605                 610                 615

ctg ctg tct gcc gag gag gcc gca aag cag aag aaa gag aag gtc tgg   2166
Leu Leu Ser Ala Glu Glu Ala Ala Lys Gln Lys Lys Glu Lys Val Trp
        620                 625                 630
```

```
gcc cac tat gag gag cag ccc gtg gag gag gtg atg cca gtg ctg gag   2214
Ala His Tyr Glu Glu Gln Pro Val Glu Glu Val Met Pro Val Leu Glu
    635                 640                 645

gag aag gag cga tct gct agc tac aag ccc gtg ttt gtg acc gag atc   2262
Glu Lys Glu Arg Ser Ala Ser Tyr Lys Pro Val Phe Val Thr Glu Ile
650                 655                 660                 665

act gat gac ctg cac ttc tac gtg cag gat gtg gag acc ggc acc cag   2310
Thr Asp Asp Leu His Phe Tyr Val Gln Asp Val Glu Thr Gly Thr Gln
                670                 675                 680

ttc cag aag ctg atg gag aac atg cgc aat gac att gcc agt cac ccc   2358
Phe Gln Lys Leu Met Glu Asn Met Arg Asn Asp Ile Ala Ser His Pro
            685                 690                 695

cct gta gag ggc tcc tat gcc ccc cgc agg gga gag ttc tgc att gcc   2406
Pro Val Glu Gly Ser Tyr Ala Pro Arg Arg Gly Glu Phe Cys Ile Ala
        700                 705                 710

aaa ttt gta gat gga gaa tgg tac cgt gcc cga gta gag aaa gtc gag   2454
Lys Phe Val Asp Gly Glu Trp Tyr Arg Ala Arg Val Glu Lys Val Glu
    715                 720                 725

tct cct gcc aaa ata cat gtc ttc tac att gac tac ggc aac aga gag   2502
Ser Pro Ala Lys Ile His Val Phe Tyr Ile Asp Tyr Gly Asn Arg Glu
730                 735                 740                 745

gtc ctg cca tcc acc cgc ctg ggt acc cta tca cct gcc ttc agc act   2550
Val Leu Pro Ser Thr Arg Leu Gly Thr Leu Ser Pro Ala Phe Ser Thr
                750                 755                 760

cgg gtg ctg cca gct caa gcc acg gag tat gcc ttc gcc ttc atc cag   2598
Arg Val Leu Pro Ala Gln Ala Thr Glu Tyr Ala Phe Ala Phe Ile Gln
            765                 770                 775

gtg ccc caa gat gat gat gcc cgc acg gac gcc gtg gac agc gta gtt   2646
Val Pro Gln Asp Asp Asp Ala Arg Thr Asp Ala Val Asp Ser Val Val
        780                 785                 790

cgg gat atc cag aac act cag tgc ctg ctc aac gtg gaa cac ctg agt   2694
Arg Asp Ile Gln Asn Thr Gln Cys Leu Leu Asn Val Glu His Leu Ser
    795                 800                 805

gcc ggc tgc ccc cat gtc acc ctg cag ttt gca gat tcc aag ggc gat   2742
Ala Gly Cys Pro His Val Thr Leu Gln Phe Ala Asp Ser Lys Gly Asp
810                 815                 820                 825

gtg ggg ctg ggc ttg gtg aag gaa ggg ctg gtc atg gtg gag gtg cgc   2790
Val Gly Leu Gly Leu Val Lys Glu Gly Leu Val Met Val Glu Val Arg
                830                 835                 840

aag gag aaa cag ttc cag aaa gtg atc aca gaa tac ctg aat gcc caa   2838
Lys Glu Lys Gln Phe Gln Lys Val Ile Thr Glu Tyr Leu Asn Ala Gln
            845                 850                 855
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gag tca gcc aag agc gcc agg ctg aac ctg tgg cgc tat gga gac ttt   2886
Glu Ser Ala Lys Ser Ala Arg Leu Asn Leu Trp Arg Tyr Gly Asp Phe
        860                 865                 870

cga gct gat gat gca gac gaa ttt ggc tac agc cgc taaggagggg        2932
Arg Ala Asp Asp Ala Asp Glu Phe Gly Tyr Ser Arg
    875                 880                 885

atcgggtttg gcccccagcc cccgtcacgc cagtccctct tcctctgccg ggagggtgtt 2992

ttcaactcca aaccccagag aggggttgta cattgggtcc agctttgctt cagtgtgtgg 3052

aaatgtctcg tggggtggca tcggggctgc ggggtgggga ccccaaggct ttctggggca 3112

gacccttgtc ctctgggatg atgggcactg ctatccacag tctctgccag ttggttttat 3172

ttggaggttt gtgggctttt ttaaaaaaaa aaaagtcctc aaatcaggaa gaaacatcaa 3232

agactatgtc ctagtggagg gagtaatcct aacacccagg ctggccgcca gctggcacct 3292

gcctctatcc cagactgccc tcgtcccagc tctctgtcca actgttgatt atgtgatttt 3352

tctgatacgt ccattctcaa atgccagtgt gttcacatct tcgctctggc cagcccattc 3412

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Ala Ala Leu Cys Glu Gly Ala Val Leu Pro Arg Ser Ala Lys Glu Leu
             20                  25                  30

Arg Cys Gln Cys Ile Lys Thr Tyr Ser Lys Pro Phe His Pro Lys Phe
         35                  40                  45

Ile Lys Glu Leu Arg Val Ile Glu Ser Gly Pro His Cys Ala Asn Thr
     50                  55                  60

Glu Ile Met
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Thr Ala Asn Pro Cys Cys Ser His Pro Cys Gln Asn Arg Gly Val Cys
             20                  25                  30

Met Ser Val Gly Phe Asp Gln Tyr Lys Cys Asp Cys Thr Arg Thr Gly
         35                  40                  45

Phe Tyr Gly Glu Asn Cys Ser Thr Pro Glu Phe Leu Thr Arg Ile Lys
     50                  55                  60

Leu Phe Leu Lys Pro Thr Pro Asn Thr Val His Tyr Ile Leu Thr His
 65                  70                  75                  80

Phe Lys Gly Phe Trp Asn Val Val Asn Asn Ile Pro Phe Leu Arg Asn
                 85                  90                  95

Ala Ile Met Ser Tyr Val Leu Thr Ser Arg Ser His Leu Ile Asp Ser
            100                 105                 110

Pro Pro Thr Tyr Asn Ala Asp Tyr Gly Tyr Lys Ser Trp Glu Ala Phe
        115                 120                 125

Ser Asn Leu Ser Tyr Tyr Thr Arg Ala Leu Pro Pro Val Pro Asp Asp
    130                 135                 140

Cys Pro Thr Pro Leu Gly Val Lys Gly Lys Lys Gln Leu Pro Asp Ser
145                 150                 155                 160

Asn Glu Ile Val Glu Lys Leu Leu Leu Arg Arg Lys Phe Ile Pro Asp
                165                 170                 175

Pro Gln Gly Ser Asn Met Met Phe Ala Phe Phe Ala Gln His Phe Thr
            180                 185                 190

His Gln Phe Phe Lys Thr Asp His Lys Arg Gly Pro Ala Phe Thr Asn
        195                 200                 205

Gly Leu Gly His Gly Val Asp Leu Asn His Ile Tyr Gly Glu Thr Leu
    210                 215                 220

Ala Arg Gln Arg Lys Leu Arg Leu Phe Lys Asp Gly Lys Met Lys Tyr
225                 230                 235                 240

Gln Ile Ile Asp Gly Glu Met Tyr Pro Pro Thr Val Lys Asp Thr Gln
                245                 250                 255

Ala Glu Met Ile Tyr Pro Pro Gln Val Pro Glu His Leu Arg Phe Ala
            260                 265                 270

Val Gly Gln Glu Val Phe Gly Leu Val Pro Gly Leu Met Met Tyr Ala
        275                 280                 285

Thr Ile Trp Leu Arg Glu His Asn Arg Val Cys Asp Val Leu Lys Gln
    290                 295                 300
```

```
Glu His Pro Glu Trp Gly Asp Glu Gln Leu Phe Gln Thr Ser Arg Leu
305                 310                 315                 320

Ile Leu Ile Gly Glu Thr Ile Lys Ile Val Ile Glu Asp Tyr Val Gln
                325                 330                 335

His Leu Ser Gly Tyr His Phe Lys Leu Lys Phe Asp Pro Glu Leu Leu
            340                 345                 350

Phe Asn Lys Gln Phe Gln Tyr Gln Asn Arg Ile Ala Ala Glu Phe Asn
        355                 360                 365

Thr Leu Tyr His Trp His Pro Leu Leu Pro Asp Thr Phe Gln Ile His
    370                 375                 380

Asp Gln Lys Tyr Asn Tyr Gln Gln Phe Ile Tyr Asn Asn Ser Ile Leu
385                 390                 395                 400

Leu Glu His Gly Ile Thr Gln Phe Val Glu Ser Phe Thr Arg Gln Ile
                405                 410                 415

Ala Gly Arg Val Ala Gly Gly Arg Asn Val Pro Pro Ala Val Gln Lys
            420                 425                 430

Val Ser Gln Ala Ser Ile Asp Gln Ser Arg Gln Met Lys Tyr Gln Ser
        435                 440                 445

Phe Asn Glu Tyr Arg Lys Arg Phe Met Leu Lys Pro Tyr Glu Ser Phe
    450                 455                 460

Glu Glu Leu Thr Gly Glu Lys Glu Met Ser Ala Glu Leu Glu Ala Leu
465                 470                 475                 480

Tyr Gly Asp Ile Asp Ala Val Glu Leu Tyr Pro Ala Leu Leu Val Glu
                485                 490                 495

Lys Pro Arg Pro Asp Ala Ile Phe Gly Glu Thr Met Val Glu Val Gly
            500                 505                 510

Ala Pro Phe Ser Leu Lys Gly Leu Met Gly Asn Val Ile Cys Ser Pro
        515                 520                 525

Ala Tyr Trp Lys Pro Ser Thr Phe Gly Gly Glu Val Gly Phe Gln Ile
    530                 535                 540

Ile Asn Thr Ala Ser Ile Gln Ser Leu Ile Cys Asn Asn Val Lys Gly
545                 550                 555                 560

Cys Pro Phe Thr Ser Phe Ser Val Pro Asp Pro Glu Leu Ile Lys Thr
                565                 570                 575

Val Thr Ile Asn Ala Ser Ser Ser Arg Ser Gly Leu Asp Asp Ile Asn
            580                 585                 590

Pro Thr Val Leu Leu Lys Glu Arg Ser Thr Glu Leu
        595                 600
```

<210> 25
<211> 360
<212> PRT
<213> Homo sapiens

<400> 25
Met Glu Asp Phe Asn Met Glu Ser Asp Ser Phe Glu Asp Phe Trp Lys
1 5 10 15

Gly Glu Asp Leu Ser Asn Tyr Ser Tyr Ser Ser Thr Leu Pro Pro Phe
20 25 30

Leu Leu Asp Ala Ala Pro Cys Glu Pro Glu Ser Leu Glu Ile Asn Lys
35 40 45

Tyr Phe Val Val Ile Ile Tyr Ala Leu Val Phe Leu Leu Ser Leu Leu
50 55 60

Gly Asn Ser Leu Val Met Leu Val Ile Leu Tyr Ser Arg Val Gly Arg
65 70 75 80

Ser Val Thr Asp Val Tyr Leu Leu Asn Leu Ala Leu Ala Asp Leu Leu
85 90 95

Phe Ala Leu Thr Leu Pro Ile Trp Ala Ala Ser Lys Val Asn Gly Trp
100 105 110

Ile Phe Gly Thr Phe Leu Cys Lys Val Val Ser Leu Leu Lys Glu Val
115 120 125

Asn Phe Tyr Ser Gly Ile Leu Leu Leu Ala Cys Ile Ser Val Asp Arg
130 135 140

Tyr Leu Ala Ile Val His Ala Thr Arg Thr Leu Thr Gln Lys Arg Tyr
145 150 155 160

Leu Val Lys Phe Ile Cys Leu Ser Ile Trp Gly Leu Ser Leu Leu Leu
165 170 175

Ala Leu Pro Val Leu Leu Phe Arg Arg Thr Val Tyr Ser Ser Asn Val
180 185 190

Ser Pro Ala Cys Tyr Glu Asp Met Gly Asn Asn Thr Ala Asn Trp Arg
195 200 205

Met Leu Leu Arg Ile Leu Pro Gln Ser Phe Gly Phe Ile Val Pro Leu
210 215 220

Leu Ile Met Leu Phe Cys Tyr Gly Phe Thr Leu Arg Thr Leu Phe Lys
225 230 235 240

Ala His Met Gly Gln Lys His Arg Ala Met Arg Val Ile Phe Ala Val
245 250 255

Val Leu Ile Phe Leu Leu Cys Trp Leu Pro Tyr Asn Leu Val Leu Leu
260 265 270

```
Ala Asp Thr Leu Met Arg Thr Gln Val Ile Gln Glu Thr Cys Glu Arg
        275                 280                 285

Arg Asn His Ile Asp Arg Ala Leu Asp Ala Thr Glu Ile Leu Gly Ile
    290                 295                 300

Leu His Ser Cys Leu Asn Pro Leu Ile Tyr Ala Phe Ile Gly Gln Lys
305                 310                 315                 320

Phe Arg His Gly Leu Leu Lys Ile Leu Ala Ile His Gly Leu Ile Ser
                325                 330                 335

Lys Asp Ser Leu Pro Lys Asp Ser Arg Pro Ser Phe Val Gly Ser Ser
            340                 345                 350

Ser Gly His Thr Ser Thr Thr Leu
        355                 360
```

<210> 26
<211> 198
<212> PRT
<213> Homo sapiens

<400> 26

```
Met Pro Leu Gly Leu Leu Trp Leu Gly Leu Ala Leu Leu Gly Ala Leu
  1               5                  10                  15

His Ala Gln Ala Gln Asp Ser Thr Ser Asp Leu Ile Pro Ala Pro Pro
             20                  25                  30

Leu Ser Lys Val Pro Leu Gln Gln Asn Phe Gln Asp Asn Gln Phe Gln
         35                  40                  45

Gly Lys Trp Tyr Val Val Gly Leu Ala Gly Asn Ala Ile Leu Arg Glu
     50                  55                  60

Asp Lys Asp Pro Gln Lys Met Tyr Ala Thr Ile Tyr Glu Leu Lys Glu
 65                  70                  75                  80

Asp Lys Ser Tyr Asn Val Thr Ser Val Leu Phe Arg Lys Lys Lys Cys
                 85                  90                  95

Asp Tyr Trp Ile Arg Thr Phe Val Pro Gly Cys Gln Pro Gly Glu Phe
            100                 105                 110

Thr Leu Gly Asn Ile Lys Ser Tyr Pro Gly Leu Thr Ser Tyr Leu Val
        115                 120                 125

Arg Val Val Ser Thr Asn Tyr Asn Gln His Ala Met Val Phe Phe Lys
    130                 135                 140

Lys Val Ser Gln Asn Arg Glu Tyr Phe Lys Ile Thr Leu Tyr Gly Arg
145                 150                 155                 160

Thr Lys Glu Leu Thr Ser Glu Leu Lys Glu Asn Phe Ile Arg Phe Ser
                165                 170                 175
```

```
Lys Tyr Leu Gly Leu Pro Glu Asn His Ile Val Phe Pro Val Pro Ile
            180                 185                 190

Asp Gln Cys Ile Asp Gly
        195
```

<210> 27
<211> 122
<212> PRT
<213> Homo sapiens

<400> 27

```
Met Lys Leu Leu Thr Gly Leu Val Phe Cys Ser Leu Val Leu Gly Val
  1               5                  10                  15

Ser Ser Arg Ser Phe Phe Ser Phe Leu Gly Glu Ala Phe Asp Gly Ala
             20                  25                  30

Arg Asp Met Trp Arg Ala Tyr Ser Asp Met Arg Glu Ala Asn Tyr Ile
         35                  40                  45

Gly Ser Asp Lys Tyr Phe His Ala Arg Gly Asn Tyr Asp Ala Ala Lys
     50                  55                  60

Arg Gly Pro Gly Gly Val Trp Ala Ala Glu Ala Ile Ser Asp Ala Arg
 65                  70                  75                  80

Glu Asn Ile Gln Arg Phe Phe Gly His Gly Ala Glu Asp Ser Leu Ala
                 85                  90                  95

Asp Gln Ala Ala Asn Glu Trp Gly Arg Ser Gly Lys Asp Pro Asn His
            100                 105                 110

Phe Arg Pro Ala Gly Leu Pro Glu Lys Tyr
        115                 120
```

<210> 28
<211> 554
<212> PRT
<213> Homo sapiens

<400> 28

```
Met Thr Ala Pro Gly Ala Ala Gly Arg Cys Pro Pro Thr Thr Trp Leu
  1               5                  10                  15

Gly Ser Leu Leu Leu Leu Val Cys Leu Leu Ala Ser Arg Ser Ile Thr
             20                  25                  30

Glu Glu Val Ser Glu Tyr Cys Ser His Met Ile Gly Ser Gly His Leu
         35                  40                  45

Gln Ser Leu Gln Arg Leu Ile Asp Ser Gln Met Glu Thr Ser Cys Gln
     50                  55                  60
```

```
Ile Thr Phe Glu Phe Val Asp Gln Glu Gln Leu Lys Asp Pro Val Cys
 65                  70                  75                  80

Tyr Leu Lys Lys Ala Phe Leu Leu Val Gln Asp Ile Met Glu Asp Thr
                85                  90                  95

Met Arg Phe Arg Asp Asn Thr Ala Asn Pro Ile Ala Ile Val Gln Leu
            100                 105                 110

Gln Glu Leu Ser Leu Arg Leu Lys Ser Cys Phe Thr Lys Asp Tyr Glu
        115                 120                 125

Glu His Asp Lys Ala Cys Val Arg Thr Phe Tyr Glu Thr Pro Leu Gln
    130                 135                 140

Leu Leu Glu Lys Val Lys Asn Val Phe Asn Glu Thr Lys Asn Leu Leu
145                 150                 155                 160

Asp Lys Asp Trp Asn Ile Phe Ser Lys Asn Cys Asn Asn Ser Phe Ala
                165                 170                 175

Glu Cys Ser Ser Gln Asp Val Val Thr Lys Pro Asp Cys Asn Cys Leu
            180                 185                 190

Tyr Pro Lys Ala Ile Pro Ser Ser Asp Pro Ala Ser Val Ser Pro His
        195                 200                 205

Gln Pro Leu Ala Pro Ser Met Ala Pro Val Ala Gly Leu Thr Trp Glu
    210                 215                 220

Asp Ser Glu Gly Thr Glu Gly Ser Ser Leu Leu Pro Gly Glu Gln Pro
225                 230                 235                 240

Leu His Thr Val Asp Pro Gly Ser Ala Lys Gln Arg Pro Pro Arg Ser
                245                 250                 255

Thr Cys Gln Ser Phe Glu Pro Pro Glu Thr Pro Val Val Lys Asp Ser
            260                 265                 270

Thr Ile Gly Gly Ser Pro Gln Pro Arg Pro Ser Val Gly Ala Phe Asn
        275                 280                 285

Pro Gly Met Glu Asp Ile Leu Asp Ser Ala Met Gly Thr Asn Trp Val
    290                 295                 300

Pro Glu Glu Ala Ser Gly Glu Ala Ser Glu Ile Pro Val Pro Gln Gly
305                 310                 315                 320

Thr Glu Leu Ser Pro Ser Arg Pro Gly Gly Gly Ser Met Gln Thr Glu
                325                 330                 335

Pro Ala Arg Pro Ser Asn Phe Leu Ser Ala Ser Ser Pro Leu Pro Ala
            340                 345                 350

Ser Ala Lys Gly Gln Gln Pro Ala Asp Val Thr Ala Thr Ala Leu Pro
        355                 360                 365
```

```
Arg Val Gly Pro Val Met Pro Thr Gly Gln Asp Trp Asn His Thr Pro
    370                 375                 380

Gln Lys Thr Asp His Pro Ser Ala Leu Leu Arg Asp Pro Pro Glu Pro
385                 390                 395                 400

Gly Ser Pro Arg Ile Ser Ser Leu Arg Pro Gln Ala Leu Ser Asn Pro
                405                 410                 415

Ser Thr Leu Ser Ala Gln Pro Gln Leu Ser Arg Ser His Ser Ser Gly
            420                 425                 430

Ser Val Leu Pro Leu Gly Glu Leu Glu Gly Arg Arg Ser Thr Arg Asp
        435                 440                 445

Arg Thr Ser Pro Ala Glu Pro Glu Ala Ala Pro Ala Ser Glu Gly Ala
    450                 455                 460

Ala Arg Pro Leu Pro Arg Phe Asn Ser Val Pro Leu Thr Asp Thr Gly
465                 470                 475                 480

His Glu Arg Gln Ser Glu Gly Ser Ser Ser Pro Gln Leu Gln Glu Ser
                485                 490                 495

Val Phe His Leu Leu Val Pro Ser Val Ile Leu Val Leu Leu Ala Val
            500                 505                 510

Gly Gly Leu Leu Phe Tyr Arg Trp Arg Arg Arg Ser His Gln Glu Pro
        515                 520                 525

Gln Arg Ala Asp Ser Pro Leu Glu Gln Pro Glu Gly Ser Pro Leu Thr
    530                 535                 540

Gln Asp Asp Arg Gln Val Glu Leu Pro Val
545                 550
```

<210> 29
<211> 107
<212> PRT
<213> Homo sapiens

<400> 29

```
Met Ala Arg Ala Ala Leu Ser Ala Ala Pro Ser Asn Pro Arg Leu Leu
  1               5                  10                  15

Arg Val Ala Leu Leu Leu Leu Leu Leu Val Ala Ala Gly Arg Arg Ala
             20                  25                  30

Ala Gly Ala Ser Val Ala Thr Glu Leu Arg Cys Gln Cys Leu Gln Thr
         35                  40                  45

Leu Gln Gly Ile His Pro Lys Asn Ile Gln Ser Val Asn Val Lys Ser
     50                  55                  60

Pro Gly Pro His Cys Ala Gln Thr Glu Val Ile Ala Thr Leu Lys Asn
 65                  70                  75                  80
```

```
Gly Arg Lys Ala Cys Leu Asn Pro Ala Ser Pro Ile Val Lys Lys Ile
                85                  90                  95

Ile Glu Lys Met Leu Asn Ser Asp Lys Ser Asn
            100                 105
```

<210> 30
<211> 106
<212> PRT
<213> Homo sapiens

<400> 30

```
Met Ala His Ala Thr Leu Ser Ala Ala Pro Ser Asn Pro Arg Leu Leu
  1               5                  10                  15

Arg Val Ala Leu Leu Leu Leu Leu Leu Val Gly Ser Arg Arg Ala Ala
            20                  25                  30

Gly Ala Ser Val Val Thr Glu Leu Arg Cys Gln Cys Leu Gln Thr Leu
        35                  40                  45

Gln Gly Ile His Leu Lys Asn Ile Gln Ser Val Asn Val Arg Ser Pro
    50                  55                  60

Gly Pro His Cys Ala Gln Thr Glu Val Ile Ala Thr Leu Lys Asn Gly
65                  70                  75                  80

Lys Lys Ala Cys Leu Asn Pro Ala Ser Pro Met Val Gln Lys Ile Ile
                85                  90                  95

Glu Lys Ile Leu Asn Lys Gly Ser Thr Asn
            100                 105
```

<210> 31
<211> 300
<212> PRT
<213> Homo sapiens

<400> 31

```
Met Arg Ile Ala Val Ile Cys Phe Cys Leu Leu Gly Ile Thr Cys Ala
  1               5                  10                  15

Ile Pro Val Lys Gln Ala Asp Ser Gly Ser Ser Glu Glu Lys Gln Leu
            20                  25                  30

Tyr Asn Lys Tyr Pro Asp Ala Val Ala Thr Trp Leu Asn Pro Asp Pro
        35                  40                  45

Ser Gln Lys Gln Asn Leu Leu Ala Pro Gln Thr Leu Pro Ser Lys Ser
    50                  55                  60

Asn Glu Ser His Asp His Met Asp Asp Met Asp Asp Glu Asp Asp Asp
65                  70                  75                  80
```

```
Asp His Val Asp Ser Gln Asp Ser Ile Asp Ser Asn Asp Ser Asp Asp
                 85                  90                  95

Val Asp Asp Thr Asp Asp Ser His Gln Ser Asp Glu Ser His His Ser
            100                 105                 110

Asp Glu Ser Asp Glu Leu Val Thr Asp Phe Pro Thr Asp Leu Pro Ala
        115                 120                 125

Thr Glu Val Phe Thr Pro Val Val Pro Thr Val Asp Thr Tyr Asp Gly
    130                 135                 140

Arg Gly Asp Ser Val Val Tyr Gly Leu Arg Ser Lys Ser Lys Lys Phe
145                 150                 155                 160

Arg Arg Pro Asp Ile Gln Tyr Pro Asp Ala Thr Asp Glu Asp Ile Thr
                165                 170                 175

Ser His Met Glu Ser Glu Glu Leu Asn Gly Ala Tyr Lys Ala Ile Pro
            180                 185                 190

Val Ala Gln Asp Leu Asn Ala Pro Ser Asp Trp Asp Ser Arg Gly Lys
        195                 200                 205

Asp Ser Tyr Glu Thr Ser Gln Leu Asp Asp Gln Ser Ala Glu Thr His
    210                 215                 220

Ser His Lys Gln Ser Arg Leu Tyr Lys Arg Lys Ala Asn Asp Glu Ser
225                 230                 235                 240

Asn Glu His Ser Asp Val Ile Asp Ser Gln Glu Leu Ser Lys Val Ser
                245                 250                 255

Arg Glu Phe His Ser His Glu Phe His Ser His Glu Asp Met Leu Val
            260                 265                 270

Val Asp Pro Lys Ser Lys Glu Glu Asp Lys His Leu Lys Phe Arg Ile
        275                 280                 285

Ser His Glu Leu Asp Ser Ala Ser Ser Glu Val Asn
    290                 295                 300
```

<210> 32
<211> 295
<212> PRT
<213> Homo sapiens

<400> 32

```
Met Glu His Gln Leu Leu Cys Cys Glu Val Glu Thr Ile Arg Arg Ala
  1               5                  10                  15

Tyr Pro Asp Ala Asn Leu Leu Asn Asp Arg Val Leu Arg Ala Met Leu
             20                  25                  30
```

```
Lys Ala Glu Glu Thr Cys Ala Pro Ser Val Ser Tyr Phe Lys Cys Val
         35                  40                  45

Gln Lys Glu Val Leu Pro Ser Met Arg Lys Ile Val Ala Thr Trp Met
     50                  55                  60

Leu Glu Val Cys Glu Glu Gln Lys Cys Glu Glu Glu Val Phe Pro Leu
 65                  70                  75                  80

Ala Met Asn Tyr Leu Asp Arg Phe Leu Ser Leu Glu Pro Val Lys Lys
                 85                  90                  95

Ser Arg Leu Gln Leu Leu Gly Ala Thr Cys Met Phe Val Ala Ser Lys
            100                 105                 110

Met Lys Glu Thr Ile Pro Leu Thr Ala Glu Lys Leu Cys Ile Tyr Thr
        115                 120                 125

Asp Gly Ser Ile Arg Pro Glu Glu Leu Leu Gln Met Glu Leu Leu Leu
    130                 135                 140

Val Asn Lys Leu Lys Trp Asn Leu Ala Ala Met Thr Pro His Asp Phe
145                 150                 155                 160

Ile Glu His Phe Leu Ser Lys Met Pro Glu Ala Glu Glu Asn Lys Gln
                165                 170                 175

Ile Ile Arg Lys His Ala Gln Thr Phe Val Ala Ser Cys Ala Thr Asp
            180                 185                 190

Val Lys Phe Ile Ser Asn Pro Pro Ser Met Val Ala Ala Gly Ser Val
        195                 200                 205

Val Ala Ala Val Gln Gly Leu Asn Leu Arg Ser Pro Asn Asn Phe Leu
    210                 215                 220

Ser Tyr Tyr Arg Leu Thr Arg Phe Leu Ser Arg Val Ile Lys Cys Asp
225                 230                 235                 240

Pro Asp Cys Leu Arg Ala Cys Gln Glu Gln Ile Glu Ala Leu Leu Glu
                245                 250                 255

Ser Ser Leu Arg Gln Ala Gln Gln Asn Met Asp Pro Lys Ala Ala Glu
            260                 265                 270

Glu Glu Glu Glu Glu Glu Glu Glu Val Asp Leu Ala Cys Thr Pro Thr
        275                 280                 285

Asp Val Arg Asp Val Asp Ile
    290                 295
```

<210> 33
<211> 439
<212> PRT
<213> Homo sapiens

<400> 33

```
Met Pro Leu Asn Val Ser Phe Thr Asn Arg Asn Tyr Asp Leu Asp Tyr
  1               5                  10                  15

Asp Ser Val Gln Pro Tyr Phe Tyr Cys Asp Glu Glu Glu Asn Phe Tyr
             20                  25                  30

Gln Gln Gln Gln Gln Ser Glu Leu Gln Pro Pro Ala Pro Ser Glu Asp
         35                  40                  45

Ile Trp Lys Lys Phe Glu Leu Leu Pro Thr Pro Pro Leu Ser Pro Ser
     50                  55                  60

Arg Arg Ser Gly Leu Cys Ser Pro Ser Tyr Val Ala Val Thr Pro Phe
 65                  70                  75                  80

Ser Leu Arg Gly Asp Asn Asp Gly Gly Gly Gly Ser Phe Ser Thr Ala
                 85                  90                  95

Asp Gln Leu Glu Met Val Thr Glu Leu Leu Gly Gly Asp Met Val Asn
            100                 105                 110

Gln Ser Phe Ile Cys Asp Pro Asp Asp Glu Thr Phe Ile Lys Asn Ile
        115                 120                 125

Ile Ile Gln Asp Cys Met Trp Ser Gly Phe Ser Ala Ala Ala Lys Leu
    130                 135                 140

Val Ser Glu Lys Leu Ala Ser Tyr Gln Ala Ala Arg Lys Asp Ser Gly
145                 150                 155                 160

Ser Pro Asn Pro Ala Arg Gly His Ser Val Cys Ser Thr Ser Ser Leu
                165                 170                 175

Tyr Leu Gln Asp Leu Ser Ala Ala Ala Ser Glu Cys Ile Asp Pro Ser
            180                 185                 190

Val Val Phe Pro Tyr Pro Leu Asn Asp Ser Ser Ser Pro Lys Ser Cys
        195                 200                 205

Ala Ser Gln Asp Ser Ser Ala Phe Ser Pro Ser Ser Asp Ser Leu Leu
    210                 215                 220

Ser Ser Thr Glu Ser Ser Pro Gln Gly Ser Pro Glu Pro Leu Val Leu
225                 230                 235                 240

His Glu Glu Thr Pro Pro Thr Thr Ser Ser Asp Ser Glu Glu Glu Gln
                245                 250                 255

Glu Asp Glu Glu Glu Ile Asp Val Val Ser Val Glu Lys Arg Gln Ala
            260                 265                 270

Pro Gly Lys Arg Ser Glu Ser Gly Ser Pro Ser Ala Gly Gly His Ser
        275                 280                 285

Lys Pro Pro His Ser Pro Leu Val Leu Lys Arg Cys His Val Ser Thr
    290                 295                 300
```

```
His Gln His Asn Tyr Ala Ala Pro Pro Ser Thr Arg Lys Asp Tyr Pro
305                 310                 315                 320

Ala Ala Lys Arg Val Lys Leu Asp Ser Val Arg Val Leu Arg Gln Ile
                325                 330                 335

Ser Asn Asn Arg Lys Cys Thr Ser Pro Arg Ser Ser Asp Thr Glu Glu
            340                 345                 350

Asn Val Lys Arg Arg Thr His Asn Val Leu Glu Arg Gln Arg Arg Asn
        355                 360                 365

Glu Leu Lys Arg Ser Phe Phe Ala Leu Arg Asp Gln Ile Pro Glu Leu
    370                 375                 380

Glu Asn Asn Glu Lys Ala Pro Lys Val Val Ile Leu Lys Lys Ala Thr
385                 390                 395                 400

Ala Tyr Ile Leu Ser Val Gln Ala Glu Glu Gln Lys Leu Ile Ser Glu
                405                 410                 415

Glu Asp Leu Leu Arg Lys Arg Arg Glu Gln Leu Lys His Lys Leu Glu
            420                 425                 430

Gln Leu Arg Asn Ser Cys Ala
        435
```

<210> 34
<211> 164
<212> PRT
<213> Homo sapiens

<400> 34

```
Met Ser Glu Pro Ala Gly Asp Val Arg Gln Asn Pro Cys Gly Ser Lys
  1               5                  10                  15

Ala Cys Arg Arg Leu Phe Gly Pro Val Asp Ser Glu Gln Leu Ser Arg
             20                  25                  30

Asp Cys Asp Ala Leu Met Ala Gly Cys Ile Gln Glu Ala Arg Glu Arg
         35                  40                  45

Trp Asn Phe Asp Phe Val Thr Glu Thr Pro Leu Glu Gly Asp Phe Ala
     50                  55                  60

Trp Glu Arg Val Arg Gly Leu Gly Leu Pro Lys Leu Tyr Leu Pro Thr
 65                  70                  75                  80

Gly Pro Arg Arg Gly Arg Asp Glu Leu Gly Gly Gly Arg Arg Pro Gly
                 85                  90                  95

Thr Ser Pro Ala Leu Leu Gln Gly Thr Ala Glu Glu Asp His Val Asp
            100                 105                 110

Leu Ser Leu Ser Cys Thr Leu Val Pro Arg Ser Gly Glu Gln Ala Glu
        115                 120                 125
```

```
Gly Ser Pro Gly Gly Pro Gly Asp Ser Gln Gly Arg Lys Arg Arg Gln
    130                 135                 140

Thr Ser Met Thr Asp Phe Tyr His Ser Lys Arg Arg Leu Ile Phe Ser
145                 150                 155                 160

Lys Arg Lys Pro
```

<210> 35
<211> 105
<212> PRT
<213> Homo sapiens

<400> 35

```
Met Met Met Gly Ser Ala Arg Val Ala Glu Leu Leu Leu Leu His Gly
  1               5                  10                  15

Ala Glu Pro Asn Cys Ala Asp Pro Ala Thr Leu Thr Arg Pro Val His
             20                  25                  30

Asp Ala Ala Arg Glu Gly Phe Leu Asp Thr Leu Val Val Leu His Arg
         35                  40                  45

Ala Gly Ala Arg Leu Asp Val Arg Asp Ala Trp Gly Arg Leu Pro Val
     50                  55                  60

Asp Leu Ala Glu Glu Leu Gly His Arg Asp Val Ala Arg Tyr Leu Arg
 65                  70                  75                  80

Ala Ala Ala Gly Gly Thr Arg Gly Ser Asn His Ala Arg Ile Asp Ala
                 85                  90                  95

Ala Glu Gly Pro Ser Asp Ile Pro Asp
            100                 105
```

<210> 36
<211> 173
<212> PRT
<213> Homo sapiens

<400> 36

```
Met Gly Arg Gly Arg Cys Val Gly Pro Ser Leu Gln Leu Arg Gly Gln
  1               5                  10                  15

Glu Trp Arg Cys Ser Pro Leu Val Pro Lys Gly Gly Ala Ala Ala Ala
             20                  25                  30

Glu Leu Gly Pro Gly Gly Gly Glu Asn Met Val Arg Arg Phe Leu Val
         35                  40                  45

Thr Leu Arg Ile Arg Arg Ala Cys Gly Pro Pro Arg Val Arg Val Phe
     50                  55                  60
```

```
Val Val His Ile Pro Arg Leu Thr Gly Glu Trp Ala Ala Pro Gly Ala
 65                  70                  75                  80

Pro Ala Ala Val Ala Leu Val Leu Met Leu Leu Arg Ser Gln Arg Leu
                85                  90                  95

Gly Gln Gln Pro Leu Pro Arg Arg Pro Gly His Asp Asp Gly Gln Arg
            100                 105                 110

Pro Ser Gly Gly Ala Ala Ala Ala Pro Arg Arg Gly Ala Gln Leu Arg
        115                 120                 125

Arg Pro Arg His Ser His Pro Thr Arg Ala Arg Arg Cys Pro Gly Gly
    130                 135                 140

Leu Pro Gly His Ala Gly Gly Ala Ala Pro Gly Arg Gly Ala Ala Gly
145                 150                 155                 160

Arg Ala Arg Cys Leu Gly Pro Ser Ala Arg Gly Pro Gly
            165                 170
```

<210> 37
<211> 468
<212> PRT
<213> Homo sapiens

<400> 37

```
Met Val Asp Thr Glu Ser Pro Leu Cys Pro Leu Ser Pro Leu Glu Ala
  1               5                  10                  15

Gly Asp Leu Glu Ser Pro Leu Ser Glu Glu Phe Leu Gln Glu Met Gly
             20                  25                  30

Asn Ile Gln Glu Ile Ser Gln Ser Ile Gly Glu Asp Ser Ser Gly Ser
         35                  40                  45

Phe Gly Phe Thr Glu Tyr Gln Tyr Leu Gly Ser Cys Pro Gly Ser Asp
     50                  55                  60

Gly Ser Val Ile Thr Asp Thr Leu Ser Pro Ala Ser Ser Pro Ser Ser
 65                  70                  75                  80

Val Thr Tyr Pro Val Val Pro Gly Ser Val Asp Glu Ser Pro Ser Gly
                85                  90                  95

Ala Leu Asn Ile Glu Cys Arg Ile Cys Gly Asp Lys Ala Ser Gly Tyr
            100                 105                 110

His Tyr Gly Val His Ala Cys Glu Gly Cys Lys Gly Phe Phe Arg Arg
        115                 120                 125

Thr Ile Arg Leu Lys Leu Val Tyr Asp Lys Cys Asp Arg Ser Cys Lys
    130                 135                 140

Ile Gln Lys Lys Asn Arg Asn Lys Cys Gln Tyr Cys Arg Phe His Lys
145                 150                 155                 160
```

```
Cys Leu Ser Val Gly Met Ser His Asn Ala Ile Arg Phe Gly Arg Met
                165                 170                 175

Pro Arg Ser Glu Lys Ala Lys Leu Lys Ala Glu Ile Leu Thr Cys Glu
            180                 185                 190

His Asp Ile Glu Asp Ser Glu Thr Ala Asp Leu Lys Ser Leu Ala Lys
        195                 200                 205

Arg Ile Tyr Glu Ala Tyr Leu Lys Asn Phe Asn Met Asn Lys Val Lys
    210                 215                 220

Ala Arg Val Ile Leu Ser Gly Lys Ala Ser Asn Asn Pro Pro Phe Val
225                 230                 235                 240

Ile His Asp Met Glu Thr Leu Cys Met Ala Glu Lys Thr Leu Val Ala
                245                 250                 255

Lys Leu Val Ala Asn Gly Ile Gln Asn Lys Glu Ala Glu Val Arg Ile
            260                 265                 270

Phe His Cys Cys Gln Cys Thr Ser Val Glu Thr Val Thr Glu Leu Thr
        275                 280                 285

Glu Phe Ala Lys Ala Ile Pro Gly Phe Ala Asn Leu Asp Leu Asn Asp
    290                 295                 300

Gln Val Thr Leu Leu Lys Tyr Gly Val Tyr Glu Ala Ile Phe Ala Met
305                 310                 315                 320

Leu Ser Ser Val Met Asn Lys Asp Gly Met Leu Val Ala Tyr Gly Asn
                325                 330                 335

Gly Phe Ile Thr Arg Glu Phe Leu Lys Ser Leu Arg Lys Pro Phe Cys
            340                 345                 350

Asp Ile Met Glu Pro Lys Phe Asp Phe Ala Met Lys Phe Asn Ala Leu
        355                 360                 365

Glu Leu Asp Asp Ser Asp Ile Ser Leu Phe Val Ala Ala Ile Ile Cys
    370                 375                 380

Cys Gly Asp Arg Pro Gly Leu Leu Asn Val Gly His Ile Glu Lys Met
385                 390                 395                 400

Gln Glu Gly Ile Val His Val Leu Arg Leu His Leu Gln Ser Asn His
                405                 410                 415

Pro Asp Asp Ile Phe Leu Phe Pro Lys Leu Leu Gln Lys Met Ala Asp
            420                 425                 430

Leu Arg Gln Leu Val Thr Glu His Ala Gln Leu Val Gln Ile Ile Lys
        435                 440                 445
```

```
Lys Thr Glu Ser Asp Ala Ala Leu His Pro Leu Leu Gln Glu Ile Tyr
    450                 455                 460

Arg Asp Met Tyr
465
```

<210> 38
<211> 505
<212> PRT
<213> Homo sapiens

<400> 38

```
Met Gly Glu Thr Leu Gly Asp Ser Pro Ile Asp Pro Glu Ser Asp Ser
  1               5                  10                  15

Phe Thr Asp Thr Leu Ser Ala Asn Ile Ser Gln Glu Met Thr Met Val
             20                  25                  30

Asp Thr Glu Met Pro Phe Trp Pro Thr Asn Phe Gly Ile Ser Ser Val
         35                  40                  45

Asp Leu Ser Val Met Glu Asp His Ser His Ser Phe Asp Ile Lys Pro
     50                  55                  60

Phe Thr Thr Val Asp Phe Ser Ser Ile Ser Thr Pro His Tyr Glu Asp
 65                  70                  75                  80

Ile Pro Phe Thr Arg Thr Asp Pro Val Val Ala Asp Tyr Lys Tyr Asp
                 85                  90                  95

Leu Lys Leu Gln Glu Tyr Gln Ser Ala Ile Lys Val Glu Pro Ala Ser
            100                 105                 110

Pro Pro Tyr Tyr Ser Glu Lys Thr Gln Leu Tyr Asn Lys Pro His Glu
        115                 120                 125

Glu Pro Ser Asn Ser Leu Met Ala Ile Glu Cys Arg Val Cys Gly Asp
    130                 135                 140

Lys Ala Ser Gly Phe His Tyr Gly Val His Ala Cys Glu Gly Cys Lys
145                 150                 155                 160

Gly Phe Phe Arg Arg Thr Ile Arg Leu Lys Leu Ile Tyr Asp Arg Cys
                165                 170                 175

Asp Leu Asn Cys Arg Ile His Lys Lys Ser Arg Asn Lys Cys Gln Tyr
            180                 185                 190

Cys Arg Phe Gln Lys Cys Leu Ala Val Gly Met Ser His Asn Ala Ile
        195                 200                 205

Arg Phe Gly Arg Met Pro Gln Ala Glu Lys Glu Lys Leu Leu Ala Glu
    210                 215                 220

Ile Ser Ser Asp Ile Asp Gln Leu Asn Pro Glu Ser Ala Asp Leu Arg
225                 230                 235                 240
```

```
Ala Leu Ala Lys His Leu Tyr Asp Ser Tyr Ile Lys Ser Phe Pro Leu
                245                 250                 255

Thr Lys Ala Lys Ala Arg Ala Ile Leu Thr Gly Lys Thr Thr Asp Lys
            260                 265                 270

Ser Pro Phe Val Ile Tyr Asp Met Asn Ser Leu Met Met Gly Glu Asp
        275                 280                 285

Lys Ile Lys Phe Lys His Ile Thr Pro Leu Gln Glu Gln Ser Lys Glu
    290                 295                 300

Val Ala Ile Arg Ile Phe Gln Gly Cys Gln Phe Arg Ser Val Glu Ala
305                 310                 315                 320

Val Gln Glu Ile Thr Glu Tyr Ala Lys Ser Ile Pro Gly Phe Val Asn
                325                 330                 335

Leu Asp Leu Asn Asp Gln Val Thr Leu Leu Lys Tyr Gly Val His Glu
            340                 345                 350

Ile Ile Tyr Thr Met Leu Ala Ser Leu Met Asn Lys Asp Gly Val Leu
        355                 360                 365

Ile Ser Glu Gly Gln Gly Phe Met Thr Arg Glu Phe Leu Lys Ser Leu
    370                 375                 380

Arg Lys Pro Phe Gly Asp Phe Met Glu Pro Lys Phe Glu Phe Ala Val
385                 390                 395                 400

Lys Phe Asn Ala Leu Glu Leu Asp Asp Ser Asp Leu Ala Ile Phe Ile
                405                 410                 415

Ala Val Ile Ile Leu Ser Gly Asp Arg Pro Gly Leu Leu Asn Val Lys
            420                 425                 430

Pro Ile Glu Asp Ile Gln Asp Asn Leu Leu Gln Ala Leu Glu Leu Gln
        435                 440                 445

Leu Lys Leu Asn His Pro Glu Ser Ser Gln Leu Phe Ala Lys Leu Leu
    450                 455                 460

Gln Lys Met Thr Asp Leu Arg Gln Ile Val Thr Glu His Val Gln Leu
465                 470                 475                 480

Leu Gln Val Ile Lys Lys Thr Glu Thr Asp Met Ser Leu His Pro Leu
                485                 490                 495

Leu Gln Glu Ile Tyr Lys Asp Leu Tyr
            500                 505
```

<210> 39
<211> 441
<212> PRT
<213> Homo sapiens

<400> 39
Met Glu Gln Pro Gln Glu Glu Ala Pro Glu Val Arg Glu Glu Glu Glu
1 5 10 15

Lys Glu Glu Val Ala Glu Ala Glu Gly Ala Pro Glu Leu Asn Gly Gly
20 25 30

Pro Gln His Ala Leu Pro Ser Ser Ser Tyr Thr Asp Leu Ser Arg Ser
35 40 45

Ser Ser Pro Pro Ser Leu Leu Asp Gln Leu Gln Met Gly Cys Asp Gly
50 55 60

Ala Ser Cys Gly Ser Leu Asn Met Glu Cys Arg Val Cys Gly Asp Lys
65 70 75 80

Ala Ser Gly Phe His Tyr Gly Val His Ala Cys Glu Gly Cys Lys Gly
85 90 95

Phe Phe Arg Arg Thr Ile Arg Met Lys Leu Glu Tyr Glu Lys Cys Glu
100 105 110

Arg Ser Cys Lys Ile Gln Lys Lys Asn Arg Asn Lys Cys Gln Tyr Cys
115 120 125

Arg Phe Gln Lys Cys Leu Ala Leu Gly Met Ser His Asn Ala Ile Arg
130 135 140

Phe Gly Arg Met Pro Glu Ala Glu Lys Arg Lys Leu Val Ala Gly Leu
145 150 155 160

Thr Ala Asn Glu Gly Ser Gln Tyr Asn Pro Gln Val Ala Asp Leu Lys
165 170 175

Ala Phe Ser Lys His Ile Tyr Asn Ala Tyr Leu Lys Asn Phe Asn Met
180 185 190

Thr Lys Lys Lys Ala Arg Ser Ile Leu Thr Gly Lys Ala Ser His Thr
195 200 205

Ala Pro Phe Val Ile His Asp Ile Glu Thr Leu Trp Gln Ala Glu Lys
210 215 220

Gly Leu Val Trp Lys Gln Leu Val Asn Gly Leu Pro Pro Tyr Lys Glu
225 230 235 240

Ile Ser Val His Val Phe Tyr Arg Cys Gln Cys Thr Thr Val Glu Thr
245 250 255

Val Arg Glu Leu Thr Glu Phe Ala Lys Ser Ile Pro Ser Phe Ser Ser
260 265 270

Leu Phe Leu Asn Asp Gln Val Thr Leu Leu Lys Tyr Gly Val His Glu
275 280 285

Ala Ile Phe Ala Met Leu Ala Ser Ile Val Asn Lys Asp Gly Leu Leu
290 295 300

```
Val Ala Asn Gly Ser Gly Phe Val Thr Arg Glu Phe Leu Arg Ser Leu
305                 310                 315                 320

Arg Lys Pro Phe Ser Asp Ile Ile Glu Pro Lys Phe Glu Phe Ala Val
                325                 330                 335

Lys Phe Asn Ala Leu Glu Leu Asp Asp Ser Asp Leu Ala Leu Phe Ile
            340                 345                 350

Ala Ala Ile Ile Leu Cys Gly Asp Arg Pro Gly Leu Met Asn Val Pro
        355                 360                 365

Arg Val Glu Ala Ile Gln Asp Thr Ile Leu Arg Ala Leu Glu Phe His
    370                 375                 380

Leu Gln Ala Asn His Pro Asp Ala Gln Tyr Leu Phe Pro Lys Leu Leu
385                 390                 395                 400

Gln Lys Met Ala Asp Leu Arg Gln Leu Val Thr Glu His Ala Gln Met
                405                 410                 415

Met Gln Arg Ile Lys Lys Thr Glu Thr Glu Thr Ser Leu His Pro Leu
            420                 425                 430

Leu Gln Glu Ile Tyr Lys Asp Met Tyr
        435                 440
```

<210> 40
<211> 742
<212> PRT
<213> Homo sapiens

<400> 40

```
Met Asp Lys Phe Trp Trp His Ala Ala Trp Gly Leu Cys Leu Val Pro
  1               5                  10                  15

Leu Ser Leu Ala Gln Ile Asp Leu Asn Ile Thr Cys Arg Phe Ala Gly
             20                  25                  30

Val Phe His Val Glu Lys Asn Gly Arg Tyr Ser Ile Ser Arg Thr Glu
         35                  40                  45

Ala Ala Asp Leu Cys Lys Ala Phe Asn Ser Thr Leu Pro Thr Met Ala
     50                  55                  60

Gln Met Glu Lys Ala Leu Ser Ile Gly Phe Glu Thr Cys Arg Tyr Gly
 65                  70                  75                  80

Phe Ile Glu Gly His Val Val Ile Pro Arg Ile His Pro Asn Ser Ile
                 85                  90                  95

Cys Ala Ala Asn Asn Thr Gly Val Tyr Ile Leu Thr Ser Asn Thr Ser
            100                 105                 110
```

```
Gln Tyr Asp Thr Tyr Cys Phe Asn Ala Ser Ala Pro Pro Glu Glu Asp
        115                 120                 125

Cys Thr Ser Val Thr Asp Leu Pro Asn Ala Phe Asp Gly Pro Ile Thr
    130                 135                 140

Ile Thr Ile Val Asn Arg Asp Gly Thr Arg Tyr Val Gln Lys Gly Glu
145                 150                 155                 160

Tyr Arg Thr Asn Pro Glu Asp Ile Tyr Pro Ser Asn Pro Thr Asp Asp
                165                 170                 175

Asp Val Ser Ser Gly Ser Ser Ser Glu Arg Ser Ser Thr Ser Gly Gly
            180                 185                 190

Tyr Ile Phe Tyr Thr Phe Ser Thr Val His Pro Ile Pro Asp Glu Asp
        195                 200                 205

Ser Pro Trp Ile Thr Asp Ser Thr Asp Arg Ile Pro Ala Thr Thr Leu
    210                 215                 220

Met Ser Thr Ser Ala Thr Ala Thr Glu Thr Ala Thr Lys Arg Gln Glu
225                 230                 235                 240

Thr Trp Asp Trp Phe Ser Trp Leu Phe Leu Pro Ser Glu Ser Lys Asn
                245                 250                 255

His Leu His Thr Thr Thr Gln Met Ala Gly Thr Ser Ser Asn Thr Ile
            260                 265                 270

Ser Ala Gly Trp Glu Pro Asn Glu Glu Asn Glu Asp Glu Arg Asp Arg
        275                 280                 285

His Leu Ser Phe Ser Gly Ser Gly Ile Asp Asp Asp Glu Asp Phe Ile
    290                 295                 300

Ser Ser Thr Ile Ser Thr Thr Pro Arg Ala Phe Asp His Thr Lys Gln
305                 310                 315                 320

Asn Gln Asp Trp Thr Gln Trp Asn Pro Ser His Ser Asn Pro Glu Val
                325                 330                 335

Leu Leu Gln Thr Thr Thr Arg Met Thr Asp Val Asp Arg Asn Gly Thr
            340                 345                 350

Thr Ala Tyr Glu Gly Asn Trp Asn Pro Glu Ala His Pro Pro Leu Ile
        355                 360                 365

His His Glu His His Glu Glu Glu Glu Thr Pro His Ser Thr Ser Thr
    370                 375                 380

Ile Gln Ala Thr Pro Ser Ser Thr Thr Glu Glu Thr Ala Thr Gln Lys
385                 390                 395                 400

Glu Gln Trp Phe Gly Asn Arg Trp His Glu Gly Tyr Arg Gln Thr Pro
                405                 410                 415
```

```
Lys Glu Asp Ser His Ser Thr Thr Gly Thr Ala Ala Ala Ser Ala His
            420                 425                 430

Thr Ser His Pro Met Gln Gly Arg Thr Thr Pro Ser Pro Glu Asp Ser
        435                 440                 445

Ser Trp Thr Asp Phe Phe Asn Pro Ile Ser His Pro Met Gly Arg Gly
    450                 455                 460

His Gln Ala Gly Arg Arg Met Asp Met Asp Ser Ser His Ser Ile Thr
465                 470                 475                 480

Leu Gln Pro Thr Ala Asn Pro Asn Thr Gly Leu Val Glu Asp Leu Asp
                485                 490                 495

Arg Thr Gly Pro Leu Ser Met Thr Thr Gln Gln Ser Asn Ser Gln Ser
            500                 505                 510

Phe Ser Thr Ser His Glu Gly Leu Glu Glu Asp Lys Asp His Pro Thr
        515                 520                 525

Thr Ser Thr Leu Thr Ser Ser Asn Arg Asn Asp Val Thr Gly Gly Arg
    530                 535                 540

Arg Asp Pro Asn His Ser Glu Gly Ser Thr Thr Leu Leu Glu Gly Tyr
545                 550                 555                 560

Thr Ser His Tyr Pro His Thr Lys Glu Ser Arg Thr Phe Ile Pro Val
                565                 570                 575

Thr Ser Ala Lys Thr Gly Ser Phe Gly Val Thr Ala Val Thr Val Gly
            580                 585                 590

Asp Ser Asn Ser Asn Val Asn Arg Ser Leu Ser Gly Asp Gln Asp Thr
        595                 600                 605

Phe His Pro Ser Gly Gly Ser His Thr Thr His Gly Ser Glu Ser Asp
    610                 615                 620

Gly His Ser His Gly Ser Gln Glu Gly Gly Ala Asn Thr Thr Ser Gly
625                 630                 635                 640

Pro Ile Arg Thr Pro Gln Ile Pro Glu Trp Leu Ile Ile Leu Ala Ser
                645                 650                 655

Leu Leu Ala Leu Ala Leu Ile Leu Ala Val Cys Ile Ala Val Asn Ser
            660                 665                 670

Arg Arg Arg Cys Gly Gln Lys Lys Lys Leu Val Ile Asn Ser Gly Asn
        675                 680                 685

Gly Ala Val Glu Asp Arg Lys Pro Ser Gly Leu Asn Gly Glu Ala Ser
    690                 695                 700

Lys Ser Gln Glu Met Val His Leu Val Asn Lys Glu Ser Ser Glu Thr
705                 710                 715                 720
```

```
Pro Asp Gln Phe Met Thr Ala Asp Glu Thr Arg Asn Leu Gln Asn Val
                725                 730                 735

Asp Met Lys Ile Gly Val
            740
```

<210> 41
<211> 489
<212> PRT
<213> Homo sapiens

<400> 41

```
Met Leu Met Arg Leu Val Leu Thr Val Arg Ser Asn Leu Ile Pro Ser
  1               5                  10                  15

Pro Pro Thr Tyr Asn Ser Ala His Asp Tyr Ile Ser Trp Glu Ser Phe
             20                  25                  30

Ser Asn Val Ser Tyr Tyr Thr Arg Ile Leu Pro Ser Val Pro Lys Asp
         35                  40                  45

Cys Pro Thr Pro Met Gly Thr Lys Gly Lys Lys Gln Leu Pro Asp Ala
     50                  55                  60

Gln Leu Leu Ala Arg Arg Phe Leu Leu Arg Arg Lys Phe Ile Pro Asp
 65                  70                  75                  80

Pro Gln Gly Thr Asn Leu Met Phe Ala Phe Phe Ala Gln His Phe Thr
                 85                  90                  95

His Gln Phe Phe Lys Thr Ser Gly Lys Met Gly Pro Gly Phe Thr Lys
            100                 105                 110

Ala Leu Gly His Gly Val Asp Leu Gly His Ile Tyr Gly Asp Asn Leu
        115                 120                 125

Glu Arg Gln Tyr Gln Leu Arg Leu Phe Lys Asp Gly Lys Leu Lys Tyr
    130                 135                 140

Gln Val Leu Asp Gly Glu Met Tyr Pro Pro Ser Val Glu Glu Ala Pro
145                 150                 155                 160

Val Leu Met His Tyr Pro Arg Gly Ile Pro Pro Gln Ser Gln Met Ala
                165                 170                 175

Val Gly Gln Glu Val Phe Gly Leu Leu Pro Gly Leu Met Leu Tyr Ala
            180                 185                 190

Thr Leu Trp Leu Arg Glu His Asn Arg Val Cys Asp Leu Leu Lys Ala
        195                 200                 205

Glu His Pro Thr Trp Gly Asp Glu Gln Leu Phe Gln Thr Thr Arg Leu
    210                 215                 220

Ile Leu Ile Gly Glu Thr Ile Lys Ile Val Ile Glu Glu Tyr Val Gln
225                 230                 235                 240
```

```
Gln Leu Ser Gly Tyr Phe Leu Gln Leu Lys Phe Asp Pro Glu Leu Leu
                245                 250                 255

Phe Gly Val Gln Phe Gln Tyr Arg Asn Arg Ile Ala Met Glu Phe Asn
            260                 265                 270

His Leu Tyr His Trp His Pro Leu Met Pro Asp Ser Phe Lys Val Gly
        275                 280                 285

Ser Gln Glu Tyr Ser Tyr Glu Gln Phe Leu Phe Asn Thr Ser Met Leu
    290                 295                 300

Val Asp Tyr Gly Val Glu Ala Leu Val Asp Ala Phe Ser Arg Gln Ile
305                 310                 315                 320

Ala Gly Arg Ile Gly Gly Gly Arg Asn Met Asp His His Ile Leu His
                325                 330                 335

Val Ala Val Asp Val Ile Arg Glu Ser Arg Glu Met Arg Leu Gln Pro
            340                 345                 350

Phe Asn Glu Tyr Arg Lys Arg Phe Gly Met Lys Pro Tyr Thr Ser Phe
        355                 360                 365

Gln Glu Leu Val Gly Glu Lys Glu Met Ala Ala Glu Leu Glu Glu Leu
    370                 375                 380

Tyr Gly Asp Ile Asp Ala Leu Glu Phe Tyr Pro Gly Leu Leu Leu Glu
385                 390                 395                 400

Lys Cys His Pro Asn Ser Ile Phe Gly Glu Ser Met Ile Glu Ile Gly
                405                 410                 415

Ala Pro Phe Ser Leu Lys Gly Leu Leu Gly Asn Pro Ile Cys Ser Pro
            420                 425                 430

Glu Tyr Trp Lys Pro Ser Thr Phe Gly Gly Glu Val Gly Phe Asn Ile
        435                 440                 445

Val Lys Thr Ala Thr Leu Lys Lys Leu Val Cys Leu Asn Thr Lys Thr
    450                 455                 460

Cys Pro Tyr Val Ser Phe Arg Val Pro Asp Ala Ser Gln Asp Asp Gly
465                 470                 475                 480

Pro Ala Val Glu Arg Pro Ser Thr Glu
                485
```

<210> 42
<211> 96
<212> PRT
<213> Homo sapiens

<400> 42

```
Met Ser Glu Ser Ser Ser Lys Ser Ser Gln Pro Leu Ala Ser Lys Gln
  1               5                  10                  15
```

```
Glu Lys Asp Gly Thr Glu Lys Arg Gly Arg Gly Arg Pro Arg Lys Gln
            20                  25                  30

Pro Pro Lys Glu Pro Ser Glu Val Pro Thr Pro Lys Arg Pro Arg Gly
        35                  40                  45

Arg Pro Lys Gly Ser Lys Asn Lys Gly Ala Ala Lys Thr Arg Lys Thr
    50                  55                  60

Thr Thr Thr Pro Gly Arg Lys Pro Arg Gly Arg Pro Lys Lys Leu Glu
65                  70                  75                  80

Lys Glu Glu Glu Glu Gly Ile Ser Gln Glu Ser Ser Glu Glu Glu Gln
                85                  90                  95
```

<210> 43
<211> 79
<212> PRT
<213> Homo sapiens

<400> 43

```
Met Ala His Lys Gln Ile Tyr Tyr Ser Asp Lys Tyr Phe Asp Glu His
  1               5                  10                  15

Tyr Glu Tyr Arg His Val Met Leu Pro Arg Glu Leu Ser Lys Gln Val
            20                  25                  30

Pro Lys Thr His Leu Met Ser Glu Glu Glu Trp Arg Arg Leu Gly Val
        35                  40                  45

Gln Gln Ser Leu Gly Trp Val His Tyr Met Ile His Glu Pro Glu Pro
    50                  55                  60

His Ile Leu Leu Phe Arg Arg Pro Leu Pro Lys Asp Gln Gln Lys
65                  70                  75
```

<210> 44
<211> 885
<212> PRT
<213> Homo sapiens

<400> 44

```
Met Val Leu Ser Gly Cys Ala Ile Ile Val Arg Gly Gln Pro Arg Gly
  1               5                  10                  15

Gly Pro Pro Pro Glu Arg Gln Ile Asn Leu Ser Asn Ile Arg Ala Gly
            20                  25                  30

Asn Leu Ala Arg Arg Ala Ala Ala Thr Gln Pro Asp Ala Lys Asp Thr
        35                  40                  45

Pro Asp Glu Pro Trp Ala Phe Pro Ala Arg Glu Phe Leu Arg Lys Lys
    50                  55                  60
```

```
Leu Ile Gly Lys Glu Val Cys Phe Thr Ile Glu Asn Lys Thr Pro Gln
 65                  70                  75                  80

Gly Arg Glu Tyr Gly Met Ile Tyr Leu Gly Lys Asp Thr Asn Gly Glu
                85                  90                  95

Asn Ile Ala Glu Ser Leu Val Ala Glu Gly Leu Ala Thr Arg Arg Glu
            100                 105                 110

Gly Met Arg Ala Asn Asn Pro Glu Gln Asn Arg Leu Ser Glu Cys Glu
        115                 120                 125

Glu Gln Ala Lys Ala Ala Lys Lys Gly Met Trp Ser Glu Gly Asn Gly
    130                 135                 140

Ser His Thr Ile Arg Asp Leu Lys Tyr Thr Ile Glu Asn Pro Arg His
145                 150                 155                 160

Phe Val Asp Ser His His Gln Lys Pro Val Asn Ala Ile Ile Glu His
                165                 170                 175

Val Arg Asp Gly Ser Val Val Arg Ala Leu Leu Leu Pro Asp Tyr Tyr
            180                 185                 190

Leu Val Thr Val Met Leu Ser Gly Ile Lys Cys Pro Thr Phe Arg Arg
        195                 200                 205

Glu Ala Asp Gly Ser Glu Thr Pro Glu Pro Phe Ala Ala Glu Ala Lys
    210                 215                 220

Phe Phe Thr Glu Ser Arg Leu Leu Gln Arg Asp Val Gln Ile Ile Leu
225                 230                 235                 240

Glu Ser Cys His Asn Gln Asn Ile Val Gly Thr Ile Leu His Pro Asn
                245                 250                 255

Gly Asn Ile Thr Glu Leu Leu Leu Lys Glu Gly Phe Ala Arg Cys Val
            260                 265                 270

Asp Trp Ser Ile Ala Val Tyr Thr Arg Gly Ala Glu Lys Leu Arg Ala
        275                 280                 285

Ala Glu Arg Phe Ala Lys Glu Arg Arg Leu Arg Ile Trp Arg Asp Tyr
    290                 295                 300

Val Ala Pro Thr Ala Asn Leu Asp Gln Lys Asp Lys Gln Phe Val Ala
305                 310                 315                 320

Lys Val Met Gln Val Leu Asn Ala Asp Ala Ile Val Val Lys Leu Asn
                325                 330                 335

Ser Gly Asp Tyr Lys Thr Ile His Leu Ser Ser Ile Arg Pro Pro Arg
            340                 345                 350

Leu Glu Gly Glu Asn Thr Gln Asp Lys Asn Lys Lys Leu Arg Pro Leu
        355                 360                 365
```

```
Tyr Asp Ile Pro Tyr Met Phe Glu Ala Arg Glu Phe Leu Arg Lys Lys
    370                 375                 380

Leu Ile Gly Lys Lys Val Asn Val Thr Val Asp Tyr Ile Arg Pro Ala
385                 390                 395                 400

Ser Pro Ala Thr Glu Thr Val Pro Ala Phe Ser Glu Arg Thr Cys Ala
                405                 410                 415

Thr Val Thr Ile Gly Gly Ile Asn Ile Ala Glu Ala Leu Val Ser Lys
            420                 425                 430

Gly Leu Ala Thr Val Ile Arg Tyr Arg Gln Asp Asp Asp Gln Arg Ser
        435                 440                 445

Ser His Tyr Asp Glu Leu Leu Ala Ala Glu Ala Arg Ala Ile Lys Asn
    450                 455                 460

Gly Lys Gly Leu His Ser Lys Lys Glu Val Pro Ile His Arg Val Ala
465                 470                 475                 480

Asp Ile Ser Gly Asp Thr Gln Lys Ala Lys Gln Phe Leu Pro Phe Leu
                485                 490                 495

Gln Arg Ala Gly Arg Ser Glu Ala Val Val Glu Tyr Val Phe Ser Gly
            500                 505                 510

Ser Arg Leu Lys Leu Tyr Leu Pro Lys Glu Thr Cys Leu Ile Thr Phe
        515                 520                 525

Leu Leu Ala Gly Ile Glu Cys Pro Arg Gly Ala Arg Asn Leu Pro Gly
    530                 535                 540

Leu Val Gln Glu Gly Glu Pro Phe Ser Glu Glu Ala Thr Leu Phe Thr
545                 550                 555                 560

Lys Glu Leu Val Leu Gln Arg Glu Val Glu Val Glu Val Glu Ser Met
                565                 570                 575

Asp Lys Ala Gly Asn Phe Ile Gly Trp Leu His Ile Asp Gly Ala Asn
            580                 585                 590

Leu Ser Val Leu Leu Val Glu His Ala Leu Ser Lys Val His Phe Thr
        595                 600                 605

Ala Glu Arg Ser Ser Tyr Tyr Lys Ser Leu Leu Ser Ala Glu Glu Ala
    610                 615                 620

Ala Lys Gln Lys Lys Glu Lys Val Trp Ala His Tyr Glu Glu Gln Pro
625                 630                 635                 640

Val Glu Glu Val Met Pro Val Leu Glu Glu Lys Glu Arg Ser Ala Ser
                645                 650                 655

Tyr Lys Pro Val Phe Val Thr Glu Ile Thr Asp Asp Leu His Phe Tyr
            660                 665                 670
```

Val Gln Asp Val Glu Thr Gly Thr Gln Phe Gln Lys Leu Met Glu Asn
675 680 685

Met Arg Asn Asp Ile Ala Ser His Pro Pro Val Glu Gly Ser Tyr Ala
690 695 700

Pro Arg Arg Gly Glu Phe Cys Ile Ala Lys Phe Val Asp Gly Glu Trp
705 710 715 720

Tyr Arg Ala Arg Val Glu Lys Val Glu Ser Pro Ala Lys Ile His Val
725 730 735

Phe Tyr Ile Asp Tyr Gly Asn Arg Glu Val Leu Pro Ser Thr Arg Leu
740 745 750

Gly Thr Leu Ser Pro Ala Phe Ser Thr Arg Val Leu Pro Ala Gln Ala
755 760 765

Thr Glu Tyr Ala Phe Ala Phe Ile Gln Val Pro Gln Asp Asp Asp Ala
770 775 780

Arg Thr Asp Ala Val Asp Ser Val Val Arg Asp Ile Gln Asn Thr Gln
785 790 795 800

Cys Leu Leu Asn Val Glu His Leu Ser Ala Gly Cys Pro His Val Thr
805 810 815

Leu Gln Phe Ala Asp Ser Lys Gly Asp Val Gly Leu Gly Leu Val Lys
820 825 830

Glu Gly Leu Val Met Val Glu Val Arg Lys Glu Lys Gln Phe Gln Lys
835 840 845

Val Ile Thr Glu Tyr Leu Asn Ala Gln Glu Ser Ala Lys Ser Ala Arg
850 855 860

Leu Asn Leu Trp Arg Tyr Gly Asp Phe Arg Ala Asp Asp Ala Asp Glu
865 870 875 880

Phe Gly Tyr Ser Arg
885

<210> 45
<211> 26
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic primer

<400> 45
agatattgca cgggagaata tacaaa 26

<210> 46
<211> 27
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic primer

<400> 46
tcaattcctg aaattaaagt tcggata 27

<210> 47
<211> 23
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic primer

<400> 47
tctgcagagt tggaagcact cta 23

<210> 48
<211> 21
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic primer

<400> 48
gccgaggctt ttctaccaga a 21

<210> 49
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic primer

<400> 49
catggcttga tcagcaagga 20

<210> 50
<211> 21
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic primer

<400> 50
tggaagtgtg ccctgaagaa g 21

<210> 51
<211> 23
<212> DNA
<213> Homo sapiens

<400> 51
caaggagctg acttcggaac taa 23

<210> 52
<211> 22
<212> DNA
<213> Homo sapiens

<400> 52
agggaagacg atgtggtttt ca 22

<210> 53
<211> 22
<212> DNA
<213> Homo sapiens

<400> 53
gggacatgtg gagagcctac tc 22

<210> 54
<211> 21
<212> DNA
<213> Homo sapiens

<400> 54
catcatagtt cccccgagca t 21

<210> 55
<211> 21
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic primer

<400> 55
aagcagcacc agcaagtgaa g 21

<210> 56
<211> 21
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic primer

<400> 56
tcatggcctg tgtcagtcaa a 21

<210> 57
<211> 22
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic primer

<400> 57
acatgccagc cactgtgata ga 22

<210> 58
<211> 21
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic primer

<400> 58
ccctgccttc acaatgatct c 21

<210> 59
<211> 23
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic primer

<400> 59
ggaattcacc tcaagaacat cca 23

<210> 60
<211> 23
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic primer

<400> 60
agtgtggcta tgacttcggt ttg 23

<210> 61
<211> 22
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic primer

<400> 61
cagccacaag cagtccagat ta 22

<210> 62
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic primer

<400> 62
cctgactatc aatcacatcg gaat 24

<210> 63
<211> 21
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic primer

<400> 63
ccaggtgctc cacatgacag t 21

<210> 64
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic primer

<400> 64
aaacaaccaa caacaaggag aatg 24

<210> 65
<211> 21
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic primer

<400> 65
cgtctccaca catcagcaca a 21

<210> 66
<211> 22
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic primer

<400> 66
tcttggcagc aggatagtcc tt 22

<210> 67
<211> 22
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic primer

<400> 67
gcagaccagc atgacagatt tc 22

<210> 68
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic primer

<400> 68
gcggattagg gcttcctctt 20

<210> 69
<211> 21
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic primer

<400> 69
ggcaccagag gcagtaacca t 21

<210> 70
<211> 23
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic primer

<400> 70
agcctctctg gttctttcaa tcg 23

<210> 71
<211> 19
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic primer

<400> 71
tggttcacat cccgcggct 19

<210> 72
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic primer

<400> 72
tggctcctca gtagcatcag 20

<210> 73
<211> 23
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic primer

<400> 73
tgaagttcaa tgcactggaa ctg 23

<210> 74
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic primer

<400> 74
caggacgatc tccacagcaa 20

<210> 75
<211> 23
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic primer

<400> 75
tggagtccac gagatcattt aca 23

<210> 76
<211> 19
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic primer

<400> 76
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<210> 77
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<220>
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